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THE QUARTERLY REVIEW of BIOLOGY

THE PROBLEM OF THE ORIGIN OF GERM CELLS

BY FLORENCE HEYS
Department of Zoology, Washington University

SINCE the time when August Weismann (1834–1914) first made a clear distinction between the soma and the germ plasm, and introduced the now familiar idea of the uniqueness and continuity of germ cells, the origin and history of definitive germ cells have become subjects of active investigation. Many have tried their hands at it and arrived at varying conclusions.

Weismann ('83, '04) based his "*Descendenztheorie*" primarily upon his work on the Hydromedusae. In 1907 Goette in a study of Hydroids found no verification for the "germinal track" of Weismann. But the hypothesis of Weismannian continuity soon gained support from work on certain invertebrates, such as the parasitic round worm, *Ascaris* (Boveri, '92), and others, where it seemed that germ cells could be traced back definitely to early segmentation stages. According to this interpretation a part of the original fertilized egg is set apart as germ plasm early in cleavage, a single cell of the four-celled embryo, in the case of *Ascaris*.

Work on the history of vertebrate germ cells dates back to Waldeyer ('70), who first observed distinguishable germ cells in the germinal epithelium, from which he supposed them to have been derived. MacLeod ('81) in the teleost, *Hippocampus*, and the needle fish (teleost), *Belone acus*, observed that the sex cells appear in the somatopleure and splanchnopleure rather late in development, and thought them to be differentiated peritoneal cells. He came to the conclusion that the genital fold originates in a group of cells on the surface of the epithelium.

Eigenmann in 1891 believed he could identify primordial germ cells in the late cleavage stages (thirty-two cell stage the earliest) of the teleost, *Micrometrus aggregatus*, but presumably no other investigator has been able to recognize germ cells in any vertebrate until after the germ layers are formed. Three years before Weismann published the *Origin of Sex Cells in the Hydromedusae*, Nussbaum ('80) had expressed the view that germ cells were segregated early in individual development and not derived from other (that is, somatic) cells, thus embodying the idea of continuity. Neither of these theories lacks supporters. Hoffman in 1886 and Dustin in 1907 confirmed Waldeyer's theory of origin from the germinal epithelium; Kuschakewitsch ('10) and Gatenby ('16) added experimental evi-

dence. Beard ('00), B. M. Allen ('06, '07, '10, '11), and Dodds ('10) upheld the early segregation theory of Nussbaum.

Waldeyer's observation of recognizably

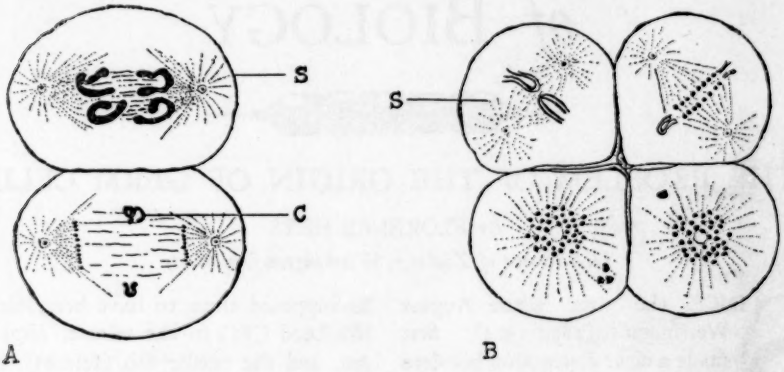

FIG. 1. EARLY CLEAVAGE OF THE EGG OF ASCARIS, SHOWING THE ORIGIN OF GERM CELLS

A—two-cell stage, the chromosomes of one cell remain intact, those in the other cell fragmented. *B*—division of four-cell stage showing three cells with fragmented chromosomes and the stem cell with chromosomes intact. *S*—stem cell from which the germ cells are derived. *C*—chromatin eliminated into the cytoplasm. Redrawn from Boveri.

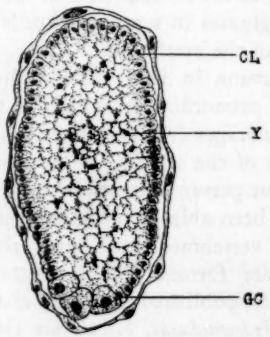

FIG. 2. DEVELOPMENT OF THE EGG OF THE FLY, MIASTOR AMERICANA, SHOWING THE CLEAVAGE CELLS AT THE PERIPHERY AND THE GERM CELLS AT THE POSTERIOR END

CL—cleavage cells. *GC*—germ cells. *Y*—yolk. After Hegner in the *Journal of Morphology*.

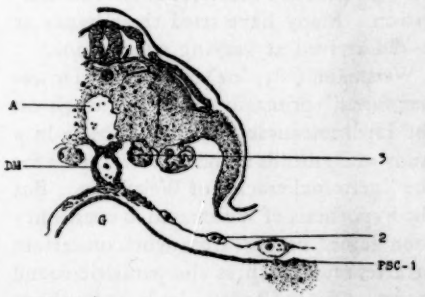

FIG. 3. SCHEMATIC SECTION THROUGH THE MIDBODY REGION OF A YOUNG EMBRYO ILLUSTRATING THE MANNER IN WHICH PRIMORDIAL GERM CELLS ARE BELIEVED TO ORIGINATE IN THE YOLK-SAC ENTODERM AND MIGRATE TO THE DEVELOPING GONAD

A—aorta. *DM*—dorsal mesentery. *G*—gut. *PSC 1*—primordial germ cells in the entoderm. *PSC 2*—primordial germ cells in the blood vessels. *PSC 3*—primordial germ cells at the site of the developing gonad. After Patten—*Embryology of the Chick*.

different cells in the germinal epithelium, together with the evidence of other workers for early segregation, suggested the possibility of tracing the so-called primordial germ cells and following their migration in the developing embryo until they reached the site of the gonad.

Basing his conclusions upon work on the mouse, Jenkinson in 1913 figured primordial germ cells and described them as forming the yolk sac and migrating to

the genital ridge. He was cautious, however, in expressing an opinion as to their ultimate fate, and admitted the possibility of peritoneal origin for some of the germ cells.

Child ('06) was convinced from work on the cestode, *Moniezia expansa*, that the germ cells develop from cells of the parenchymal syncytium, which must be regarded as composed of differentiated tissue cells. In connection with the development of his theory of differentiation ('15) he says:

> In the tapeworm, *Moniezia*, for example, the sex cells arise from the parenchyma and apparently any parenchymal cells which lie within the region involved in the production of sex cells may undergo dedifferentiation and take part in the process. Even the large muscle cells may give rise to testes. . . . . In such cases the muscle fibre undergoes degeneration, the vacuoles disappear, and the nucleus begins to divide. ('15, p. 331).

Fuss ('11, '13) upon the basis of Rubaschkin's ('08, '10) proposed method of differential staining of germ cells, located what he identified as "*extraregionare Geschlechtzellen*" in the intestinal epithelium of the four-weeks human embryo (quoted by Simkins, '28). The supposed sex cells were arranged in such a way as to suggest an active migration from the entoderm of the gut into the visceral peritoneum.

Felix ('12), who may or may not have been influenced by Rubaschkin's differential coloration method, distinguished two categories of germ cells in the course of gametogenesis. These he designated as primary and secondary genital cells. The primary genital cells, he contended, had a special origin from the segmentation cells, and were, therefore, extra-regional in origin, that is, they arose directly from the blastomeres of early cleavage and remained distinctly reproductive cells, destined to migrate into the developing gonad. But these cells, after so careful a preservation, were found to degenerate and contribute nothing to the definitive germ-cell population. The secondary genital cells, Felix believed, were derived from the peritoneum of the gonads, and these passed through growth and maturation processes into ova or sperm, as the case might be. The two categories of cells had no physiological or genetic connection.

De Winiwarter and Sainmont ('09) from studies of germ cells of embryos and kittens, also maintained that the primordial germ cells in the cat all degenerate and are replaced by a proliferation from the germinal peritoneum. De Winiwarter later ('10) declared that a like fate could be demonstrated for primordial germ cells in man.

Thus it is admitted by many that the so-called primordial germ cells *do appear* in early embryonic stages, and, when first distinguishable, are in the gut entoderm. From there they migrate to the genital ridge, such cells being the preprimordium of the gonad.

At the time of these relatively early investigations, the last word by no means had been said on the origin of the definitive procreation cells. Many cytological contributions have appeared in recent years, favoring continuity from generation to generation, and, by inference, at least, supporting the hypothesis that all germ cells now in existence go back in an unbroken line to the germinal materials of the first living thing upon the earth.

Others find evidence in favor of the view that a discontinuity of germ cells exists between the generations, each crop of definitive germ cells arising anew from the peritoneum of the gonads. The conclusions arrived at in these later investigations place their authors readily in four groups:

I. Those who deny early segregation of germ cells, and believe that germ-cell formation is a matter of the differentiation of somatic cells.

II. Those who admit early segregation of germ cells, but conclude that such cells are not definitive and degenerate, to be replaced by proliferations of new cells from the germinal epithelium.

III. Those whose investigations have led to the conclusion that germ cells are segregated early and migrate to the site of the developing gonad. These persist as definitive germ cells, but their numbers are increased periodically by a proliferation from the epithelium.

IV. Those who believe that the definitive germ cells are set aside at an early stage in embryonic development not to be replaced later by transformation of differentiated peritoneal cells. Their numbers are increased only by mitotic divisions.

GROUP I

From the standpoint of a study of cellular embryonic structure and of cell migration, this group of investigators fails to find in the history of germ cells, the continuity upon which adherents of the Weismannian hypothesis lay stress. They deny segregation entirely; primordial germ cells, as such, do not exist. Many of them consider the large cells so often observed by workers and called primordial sex cells, to be merely somatic cells in different phases of metabolic activity. It has been suggested that their enlargement is preparatory to cell division, or that they are cells which are enlarged because of being, for some reason, retarded in their division and which, therefore, have a longer resting (storage) period. The question of the formation of germ cells becomes thus purely a matter of differentiation of somatic cells.

The work of Hargitt

Of particular interest in this connection is the work of Hargitt ('13, '16, '17, '18, '19, '24, '25, '26), since it includes studies from both invertebrates and vertebrates. The early work of Hargitt was on the origin of germ cells in Coelenterates. These results were presented in a series of papers from 1913 to 1919. From this work he concluded that germ cells are not segregated early in ontogeny and kept isolated until the time of maturity, but are differentiated at a time just preceding sexual maturity; and that they may arise directly from functional body cells.

The application of these results Hargitt considered rather far-reaching: namely, that the germ-plasm theory would have to be discarded, in so far, at least, as it related to the lower invertebrates, and it was suggested that eventually it might be discarded for the vertebrates as well. With his abandonment of the germ-plasm theory, the conclusion follows that there is fundamentally no distinction between germ cells and body cells.

After the publication of these results several writers on this and related subjects intimated that, while these conclusions might well apply to such simply-organized animals as the Coelenterates, they could hardly be referred to the highly-organized vertebrates. Hargitt, very possibly influenced by these suggestions, sought to extend his studies to the higher forms.

In 1924 Hargitt's paper appeared describing the origin of germ cells in the adult salamander, *Diemyctylus viridescens*. Here he suggested that the problem of the origin of germ cells in vertebrates might be divided into two phases. One is concerned with the earliest appearance and source of the primordial germ cells in ontogeny and their fate. The second phase deals with the relation of these to the germ cells of the adult which periodically produce the functional germ cells, as is true in those forms such as the salamander, where seasonal regeneration of the gonad seems to take place. Hargitt's

work on *Diemyctylus* dealt only with this second phase.

The program followed was the critical examination of the tissues of the testis: the stroma, the young cysts containing spermatogonia and spermatocytes, the cysts containing spermatozoa, older degenerating cysts, interstitial cells, the germinal epithelium and peritoneum of the neighboring regions outside the testis. Hargitt considered that these categories include all possible sources of germ-cell origin in the adult.

In the stroma of the testis (connective tissue) scattered, isolated cells were observed and identified as spermatogonia. Such cells were always found near the collecting ducts and in the stroma between the cysts. Hargitt identified these as germ cells by their size, differential staining behavior, and the fact that in some cases they were enclosed by a capsule of the stroma; but chiefly by the presence of a polymorphic nucleus, in this case bilobed. The presence of an attraction sphere was also used as an additional criterion of a germ cell.

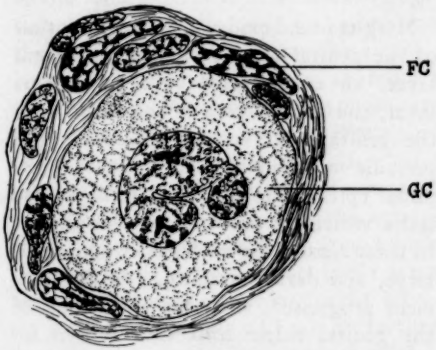

FIG. 4. GERM CELL WITH FOLLICLE CELL FORMING; BILOBED NUCLEUS CONSPICUOUS

FC—follicle cell. *GC*—germ cell. After Hargitt in *Jour. Morph.*

Since these germ cells were found in the stroma, it suggested to him that they are stroma cells differentiated into germ cells. Hargitt was of the opinion that their consistent, close association with adjacent collecting ducts is of the greatest significance. He did not consider for a moment that these were primordial, residual germ cells, but they must be a new generation of germ cells whose origin was the epithelial cells of the collecting ducts, since in all cases they were found in close proximity to the terminal branch of the duct. He observed mitosis going on in the peritoneum surrounding the testis and considered this a second source of the new generation of germ cells. But these cells from the epithelium migrate, after division, into the stroma and are later transformed into spermatogonia. In the process of differentiation, cells of the peritoneum seemed to take on first the typical polymorphic nucleus, which was considered the infallible sign of a germ cell in these tissues. These cells could be traced into the stroma. The appearance of the polymorphic nucleus was conspicuous and constituted the initial step in germ-cell transformation.

As a result of these studies in the salamander, their author concluded that what had been true for the Coelenterates was also true for the vertebrates, in so far, at least, as *Diemyctylus* was concerned. If germ cells are early segregated, they must degenerate, for he found no trace of them in the adult. It, therefore, seemed logical to Hargitt to discard all previous views of the distinction between germ cells and body cells and the concept of germ-cell continuity.

Recently ('25, '26) two papers by Hargitt have completed the series. They carry the study into the mammals and treat of the first phase of the problem, that is, the earliest appearance and source

of primordial germ cells, if there be such, and the question of their ultimate destination. Hargitt indicates that a reliable answer to this question can come only from a careful study of the germ cells through the entire period of ontogeny, from their first appearance in the embryo until maturity. He undertook to make such a study in the albino rat. Using data given by Huber ('15) on the early development of the rat "1st day after insemination—ovum contains male and female pronuclei; 3rd day after insemination—four-celled stage of cleavage; 5th day—

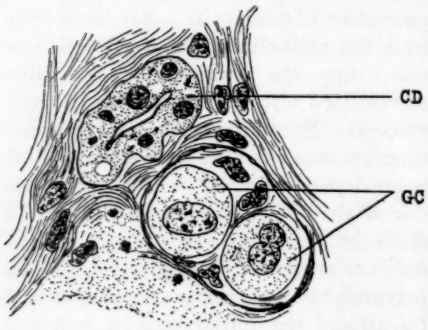

FIG. 5. A CYST CONTAINING TWO GERM CELLS SHOWN IN CLOSE PROXIMITY TO THE COLLECTING DUCT

CD—collecting duct. *GC*—germ cell. After Hargitt in *Jour. Morph.*

early blastodermic vesicle; etc.", Hargitt selected for study stages beginning with the primitive streak stage (9th day), a search being made for what might prove to be primordial germ cells.

Large cells of different staining reaction were found in the epithelial mesoderm, but these were also present in the ectoderm, the entoderm of the gut, and even in the extra-embryonic tissues. There was no distinction between these larger cells, wherever found. Hargitt points out that other workers, especially Woods ('02), observed a wide distribution of these large cells: quoting Woods, "In the youngest embryo studied, in the blastoderm stage, practically all the cells, except those in the ectoderm, had all the characteristics of the primitive ova found in later embryos of from one to six millimeters." Hargitt says,

> With such a universal distribution, it is hard to look upon them as germ cells, but this wide-spread diffusion would be entirely in accord with the view that they are merely enlarged local cells which have missed some cell division. . . . . This would mean a lack of difference between germ cells and body cells, with a later differentiation of both from the embryonic tissues.

Hargitt found evidence of the formation of the genital ridge from the peritoneal layer, an enlargement of cells in this layer, and a wandering of these cells into the genital-ridge region, similar to the periodic migration of cells from the germinal epithelium into the stroma of the testis which he observed in *Diemyctylus*. In these tissues the nuclei were spherical, large, and darkly-staining. As development progressed, from the thickening of the genital ridge until the twelfth or thirteenth days, when the gonad is truly distinguishable, the large cells in other regions, ectoderm, extra-embryonic membranes, entoderm and mesenchyme, disappeared, while the proportion of darkly-staining cells with plump, spherical nuclei increased in the genital ridge and nearby peritoneum. Only very rarely were large cells found between the kidney, aorta, genital ridge, and the gut. Hargitt explained the disappearance of these cells in the following way: all the retarded cells (large cells) which were observed earlier and had so wide a distribution are now, in the twelfth and thirteenth-day embryos, actively dividing, and the only large cells left are those differentiating from the peritoneum—the

germ cells. At this time only a clumping together of the large cells within the genital ridge was apparent, an observation which Hargitt considered of great importance.

In the earlier work, on *Diemyctylus*, Hargitt had used the appearance of the polymorphic nucleus as the criterion of a germ cell, but from these studies he concluded that there is no single distinguishing characteristic or group of characteristics; the only satisfactory method, he says, is to trace the germ cells back step by step. In the rat such a procedure led him to the conclusion that there is no segregation of germ cells and no migration through a "germ track" into the gonad.

Hargitt's most recent paper ('26) reports the results of his work on the male rat, from the fourteenth day in embryonic development to maturity. After the fourteenth day the testis differentiated from the indifferent gonad by the separation of a definite surface layer, from which the sex cords arise. These cords were found to increase and grow by the activity of their own cells and not by further contributions from the germinal epithelium. The remainder of the history of the testis was purely a question of gradual differentiation. (Since the writing of this review Hargitt has extended his studies to the female rat with identical conclusions ('29) .)

As a result of his studies on germ-cell origin and history, Hargitt is willing to discard entirely the concept of continuity: "Personally, I believe biology would be greatly the gainer by dropping the germplasm idea entirely and permanently." ('26, p. 290).

The Work of Firket

Firket ('14, '20) is of the opinion that the cytological aspect of mitochondria, used by some workers, particularly Rubaschkin ('10, '12) and Tschaschin ('10), is an unreliable criterion of germ cells, but finds it a convenient method for following these cells in their development. He concluded that in the chick most of the primary germ cells both of the ovary and testis eventually degenerated, and that the majority of definitive ova or spermatozoa were derived from the epithelial organs of the sex glands. Since these constituted a second generation of germ cells, they were called secondary germ cells. Nevertheless, Firket saw no reason why "certain of the primary germ cells might not produce some of the definitive cells, since it was impossible to distinguish between primary and secondary cells." ('20, p. 311).

In contrast to what he described in the chick, Firket found, in a study of the testis of young rats, that the two generations of germ cells could be distinguished from each other very easily, because the cells of the second generation, called secondary cells, arose only when those of the first generation, the primary cells, had entirely disappeared. Primary germ cells in the chick developed at least until the growth period, reaching well-characterized stages of preparation for maturation divisions. But in the rat he found no evidence that primary cells ever reached the period of growth, all apparently degenerating at an earlier stage.

The bearing of sex-reversal on the origin of germ cells

Studies on sex-reversal have been considered by some an important source of evidence in favor of the origin of definitive germ cells from the epithelium. Essenberg ('23, '26) in work on sex-reversal in the teleost, *Xiphophorus helleri*, reported germ-cell formation from the epithelium of the "ovarian cavity" after degeneration

of the ovary. Whatever the cause of this degeneration its occurrence has been demonstrated experimentally. The large oocytes disintegrated first, followed shortly by the medium cells, and finally by the very young oocytes, located close to the epithelium. The epithelial covering of the ovary completely disintegrated, but the epithelium of the so-called "ovarian cavity" was not subject to the disintegration process. After a period of rest, this epithelium again became active and proliferated germ cells which formed, by means of sex cords and later seminiferous tubules, a gonad of the opposite sex. Essenberg arrived at the conclusion that definitive germ cells in the teleost are not linear descendants of primordial germ cells, but originate from the peritoneum, and that the new gonad of the transforming fish arises from a part of this peritoneum: "It is interesting to note that the epithelium of the ovarian cavity which gives rise to the definitive male cells originates . . . . from the peritoneum of the body cavity." ('26, p. 101).

Similar results were obtained in the fowl by Fell ('23), who studied gonads of eight birds representing various stages in sex-reversal from female to male. This author also found germ cells of the opposite sex proliferating from the peritoneal epithelium of the degenerating ovary. Cells from the sex cords gave rise later to seminiferous tubules, and finally to functional sperm.

No explanation is offered by either of these authors for the phenomenon of sex-reversal. Essenberg suggests that the factors must "reside in the gonad and possibly in the germ cells themselves." Until more is known of the causative factors in sex-reversal, the source of the cells which go to make up the transformed gonad remains a question.

The work of Simkins and others

Work by Simkins in 1923 on the mouse substantiated Hargitt, though Simkins was a little more ready to admit the possibility of germ-cell continuity than Hargitt. Simkins states that there is no segregation of germ cells and that none of the so-called primordial germ cells of early embryos migrates or has anything to do with the formation of the gonad. The large cells, so frequently seen, are not germ cells at all, but very active cells participating in the formation of other organs. Germ cells come only from the coelomic epithelium as it produces the genital thickening.

Kohno ('25) working on the "*Keimbahn*" of man recognized what he considered germ cells in the lateral plates of mesoderm of a 2.3-millimeter embryo, and as these plates were folded under the gut in 2.8-millimeter embryos, the germ cells moved up into the epithelium of the gut and mesentery, from which they migrated farther into the developing gonads in embryos measuring five to seven millimeters. But Simkins suggests the possibility that Kohno's "*Urgenitalzellen*" are somatic cells in different phases of activity or perhaps artifacts due to staining.

On the basis of his work on the mouse Simkins hesitates to discard the concept of continuity, but in a later paper ('28) on the origin of sex cells in man, he indicates his confidence in the conclusion that no strict independence of somatic and germ cells is demonstrable. Cytological examinations were made of human embryos of both sexes, measuring from 2.6 millimeters to twenty-five millimeters, when the gonad is definitely formed. Simkins considers the supposed germ cells to be liquified areas, surrounding a mitotic or degenerating nucleus, which have taken stain. He believes that the definitive

cells of both ovary and testis come from the smaller cells of the gonad, whose origin is from the peritoneum, and thus are transformed somatic cells. The suggestion is made that if the original germinal peritoneum is removed, no more cells will be produced, but if the gonad can be removed without the peritoneum then why not germ cells replaced by transformed soma cells? This suggestion indicates the relation of regeneration of gonads to the problem of germ-cell continuity, a study of which, as will be evident later, throws some light on the problem of continuity.

Very recently ('29) Wolf has concluded from studies of *Platypoecilus maculatus* that the epithelial cells of the lining of the ovarian cavity transform into germ cells.

GROUP II

A second group of investigators includes those who observe the large, primordial germ cells and admit early segregation, but find no evidence of their persistence and therefore conclude that such cells are not definitive and degenerate to be replaced by proliferations of new cells from the germinal epithelium.

Perhaps the first to come to this conclusion was Mihalkovics, who in 1885, after a study of *Amniotes*, stated that prominent, early-appearing cells, which might be taken for germ cells, degenerate or disappear by division into smaller cells. These were different, he said, from the real primordial germ cells, which appeared later, and should not be confused with them. And Minot in 1894 expressed doubt that such cells had any relation to the genital region or could be looked upon as primordial germ cells, since they were correlated with cell division and disappeared long before germ cells were differentiated.

Von Berenberg-Gossler in work on birds ('12) and later ('14) on reptiles reported recognizable germ cells differentiating from the genital anlage coincident with its development. He believed that any large cells appearing before the gonads developed were not germ cells but participants in a late formation of mesenchyme. Von Berenberg-Gossler demonstrated the unreliability of the criterion proposed by Rubaschkin ('10, '12) and Tschaschin ('10) that a specific type of mitochondria is characteristic of germ cells.

Kingsbury ('13, '14) contended that in the cat proliferations of germ cells from the peritoneum take place up to thirty-three days post-partum, and that by this time most of the cells have passed through meiotic phases. He found no such proliferation just before the advent of sexual maturity, nor any periodic activity of the epithelium. The first proliferation, up to thirty-three days after birth, according to Kingsbury, gives rise to the definitive oocytes.

Kingery ('17) distinguished two separate formations of germ cells from the epithelial covering of the ovary in the white mouse. The oocytes of the embryonic proliferation remain for some time in the germinal peritoneum in a resting condition. These cells pass through phases of meiosis into a second resting stage before sinking into the stroma of the ovary and taking part in follicle formation. At birth the process has become retarded, and meiotic stages are to be found only in the epithelium itself. Kingery reported a second proliferation of cells beginning at three to four days before birth and continuing until thirty to forty-five days after birth.

According to Kingery's interpretation the true oocytes are of this second proliferation in contra-distinction to the cells of the first proliferation, all of which degenerate. He claims to have traced the

definitive germ cells from their inception in the germinal epithelium until they were ready for maturation, and up to the time when graafian follicles developed. Kingery takes issue in this report with de Winiwarter and Sainmont, and some others, who make meiotic phases the criterion of a true germ cell. The ultimate destination of a cell, he says, is the only reliable criterion, and when the ovary attains maturity, the germinal potentiality of the peritoneal cells is lost.

The work of Butcher

Butcher ('27) has made a study of the white rat with a view to determining whether ova are formed after birth and during sexual maturity from the epithelial covering of the ovary. Examination was made of the ovary and tissue immediately surrounding it at intervals from birth until adult life; and meiotic phases were observed up to the third day after birth. Soon, however, particularly the third and fourth days, a condition of degeneration was seen, affecting first the cytoplasm of the cells, the nucleus merging into a resting stage. A possible explanation for this regressive process, Butcher thinks, was the crowded condition of the ovary at this stage and the consequent inadequate blood supply. This process of degeneration was especially evident about the seventeenth day, when large cavities were seen in the follicles. Butcher believes that these germ cells which are so prominent at birth disappear long before the advent of maturity and that none ever persists to become a definitive ovum.

About the sixth to seventh days, while the degeneration process was progressing among the older germ cells, he observed certain small cells of the epithelial covering begin to enlarge. Quite frequently two such cells were seen to enlarge side by side as if they were daughter cells of one small cell through mitosis. The nuclei, which formerly had been oval, began to enlarge and become spherical in form; the chromatin clumped together and stained more intensely. These young oocytes, for such they were considered, took on a spherical shape and gradually became pushed into the tunica, as definitive germ cells.

Butcher finds definite evidence that "a continuous proliferation and formation of germ cells goes on until about sixty-five days after birth, when the process becomes slightly retarded." Ovulation, of course, occurs before this time, since large corpora lutea are found. Contrary to the opinion of Kingery, Butcher believes that the germinal potentiality of the peritoneum is not lost at puberty:

> . . . . in fact, at some stages during post-pubertal life the process of the formation of germ cells is very marked. It would seem that such a condition must exist, since evidence, as interpreted by the writer, is steadily increasing that all follicles are relatively short-lived, and it is now considered by some untenable to conceive of eggs lasting the life-time of the individual ('27, p. 20).

The formation of germ cells from the epithelial covering of the ovary, according to Butcher, continues to take place until fecundity is lost at old age. A notable increase in mitotic activity in the epithelium was evident during oestrus. Cells enlarging in the epithelium were usually more common as the oestrous period approached than they were immediately following. The cells, likewise, seemed to lie deeper in the cortex as time progressed after each oestrous period. Butcher came to the conclusion that ". . . . the process of germ-cell formation in the rat from the germinal epithelium, therefore, seems to be a continuous process throughout life."

A later ('28) study of germ-cell origin extended these conclusions to the lake

lamprey, *Petromyzon marinus unicolor*, with the exception that in this species the potentiality of the epithelium seemed to be lost gradually after the formation of the gonad, as no continuous proliferation process could be detected in the adult.

McCosh ('28) made studies of a series of ontogenetic stages in *Amblystoma maculatum* from cleavage until metamorphosis. Primordial germ cells, first located in the lateral mesoderm, were traced to a definitive position in the genital anlagen. Comparative counts of these cells in younger and more advanced stages gave evidence that few ever reach the site of the developing generative gland. McCosh believes that a few of these may survive, but that the majority of the procreation cells are of somatic origin. She describes the transformation of "small cuboidal or spindle-shaped cells with oval nuclei into large germ cells with immense polymorphic or lobate nuclei," an observation in agreement with that of Hargitt ('24) in *Diemyctylus*. These cells were abundant in all older individuals. "Successive stages in the evolution of a somatic cell into a reproductive cell" involve "an increase in size, changes in shape, and a new distribution of chromatin material."

GROUP III

A third group includes papers supporting the conclusion that germ cells are set apart early, migrate to the site of the developing ovary or testis and *persist*, their numbers being increased periodically by a proliferation from the epithelium.

Bohi ('04), who worked on the trout and the salmon, came to the conclusion that some of the germ cells are set apart early in development while others arise from the epithelial cells after the genital ridge is formed. He believed that the changing of epithelial cells into genital cells lasted for a brief period only, for in embryos of 277 days or more, no transition cells were found. The number of germ cells was counted at different stages: from four to six in embryos of twenty-five days to twenty to fifty-four at 185 days after fertilization, at which the number remained fairly constant. After the 185 day mark was past a very rapid increase was observed (373 at 199 days), and was attributed to the transformation of peritoneal cells into germ cells. Bohi believed that the coelomic cells gave rise to indifferent cells, follicle cells, and germ cells; the cells on the sides of the genital fold gradually becoming transformed into germ cells.

Arai ('20) was perhaps the first to suggest continuous proliferation. In a statistical study of the post-partum history of the ovary in the rat, investigating particularly the number of ova at various ages, Arai states that the process of proliferation of new ova is most marked during the period from fifteen to sixty days, and may continue for a year after birth, although it proceeds at a much slower rate after maturity is attained. The degenerative process, which is constantly going on in the ovary, involving both primitive and definitive ova, is compensated by a continuous proliferation from the epithelium. The new cells grow, sink into the tunica albuginea and finally into the underlying stroma.

Allen ('22, '23) from careful studies of the oestrous cycle of the white mouse was led to the conclusion that at each normal oestrous period, young ova are added to the cortex of the adult ovary. He described them as arising from dividing cells in the germinal epithelium. If the angle of the cell undergoing mitosis to the surface of the ovary was more than thirty degrees, the proximal of the two daughter cells was considered to be cut off from the germinal epithelium and soon surrounded by a ring of adjacent epithelial cells.

Butcher, however, in 1927, found no verification of the observation that cells cut off with their long axes perpendicular to the surface necessarily become oocytes.

Cowperthwaite ('25), whose work will be discussed in Group IV, takes issue with Allen for lack of comparison between the appearance of the chromatin in young ova arising by proliferation of the germinal epithelium, and that in ova found before puberty. Cowperthwaite considered the meiotic phenomena of great importance, but Allen apparently observed none and deemed their absence a matter of no significance.

When mitosis was at its height, a statistical study of the proportion of very young oocytes in the cortex to slightly older ones led Allen to the belief that the cell divisions of the germinal peritoneum formed the germ cells but not the somatic tissue or stroma of the ovary. He found that there is present in the adult ovary shortly after each oestrous period a greater number of young oocytes than are observable after the dioestrous interval.

According to Allen the germ-cell population is added to periodically: "A cyclical proliferation of the germinal epithelium gives rise to a new addition of young ova to the cortex of the adult ovary at each normal oestrous period" ('23, p. 467). Allen's conclusions are thus contrary to those of Kingery that the germinal potentiality of the peritoneal cells is lost as the ovary attains maturity.

After studying a large number of ovaries from guinea pigs of various ages, including embryos and adults, Papanicolaou ('25) stated that there is a continuous process of oogenesis from the time of gonadial differentiation in the embryo up to the time of the cessation of sexual activity in the older females. The process gradually decreased with the increasing age of the individual. Papanicolaou observed, however, that at certain periods, especially during sexual maturity, a very marked activity of the epithelium was evident, resulting in the proliferation of many cells. This unusual periodicity he attributed to various "nutritive and hyperemic conditions" at these particular times.

The conclusions of Papanicolaou are in agreement with those of Butcher in so far as they subscribe to a continuous process of oögenesis.

In investigating the morphogenesis of the indifferent gonad and of the ovary, Brambell ('27) observed the usual large cells which have come to be called primordial germ cells. These were present in the primordium of the germinal ridge before the onset of epithelial proliferation, and were found in the mesentery of the gut and in the mesenchyme, near the germinal ridge, as well as in the germinal ridge, until the gonad had become "constricted off" from the surrounding peritoneum. Contrary to the experience of many, Brambell found no signs of degeneration. These early cells appeared to persist and to undergo maturation phases, and there was a marked absence of such cells from other parts of the embryo. But beside these Brambell found germ cells forming from the epithelial cells of the genital ridge:

> Every intermediate stage between the undoubted germ cells and the undifferentiated germinal epithelial cells can be seen in a single section. The cytological evidence for the formation of the "primordial" germ cells in the germinal ridge is, therefore, satisfactory.
>
> Furthermore, even if it were established that the primordial germ cells migrate into the germinal ridge from elsewhere,

and Brambell's own work brought some evidence that such was the case,

> it would still be impossible to deny that others in every way indistinguishable from them were differentiated from the epithelial cells. It would be difficult to imagine a sufficient number of germ cells

migrating to account for the rapid increase in the number found in the gonad between the tenth and twelfth days, although many of those in the gonads are in mitosis ('27, p. 403–404).

GROUP IV

There is a fourth group of writers who uphold early segregation of germ cells as well as a strict independence of germ cells and somatic cells. These are the true adherents to the principle of Weismannian continuity who believe that the germ cells are set aside at an early stage in embryonic development, not to be duplicated or replaced later by transformed peritoneal cells. In this group belong investigations which have led to the conclusion that the sole source of definitive sex cells is the primordial germ cells, appearing in early segmentation stages. These cells, first recognizable, as a rule, in the gut entoderm migrate to the site of the gonad, where they increase in number by cell division only (see Fig. 3).

In a preliminary study of *Phrynosoma cornutum* (the horned toad), Jarvis ('08) traced the path of normal migration of germ cells from the entoblast of the vascular area of the blastoderm to the yolk stalk, intestine and sclerotome of the mesentery, and thence to the germinal anlagen. Many germ cells "lose their way" along this path. These "lost cells" thus come to lie in various parts of the embryo and soon degenerate. In general the conclusions of Jarvis substantiate Beard ('00). She states that the possibility that these degenerating cells in various regions of the embryo might be transitional forms between soma and germ cells seems precluded by the fact that they were never found in what she termed the path of normal migration, and especially by their absence from the germinal anlagen.

King, also in 1908, located early germ cells in the entoderm of the Anuran, *Bufo lentiginosus*, and believed that the definitive germ cells arose only from primordial cells segregated early in development, but that peritoneal cells gave rise to all other elements of the sex gland. According to King, cyst formation takes place, but the cells of a cyst do not necessarily divide simultaneously. The cysts showed no evidence of fragmentation as has been observed by other writers on Anuran germ cells. King was led to the conclusion that in the female all the cells of a given cyst were descendants of a single, primary oogonium.

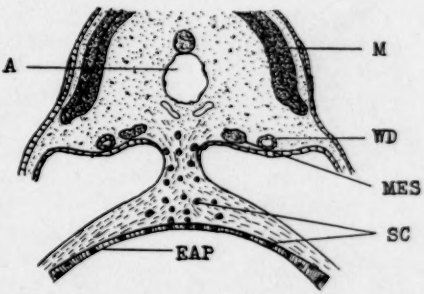

FIG. 6. DIAGRAMMATIC REPRESENTATION OF THE PATH OF GERM-CELL MIGRATION IN THE TURTLE, CHRYSEMYS MARGINATA

A—aorta. *M*—myotome. *EAP*—entoderm of the area pellucida. *WD*—Wolffian duct. *MES*—mesonephros. *SC*—sex cells. After Hegner in *The Germ-Cell Cycle in Animals*.

The work of Hegner

According to Hegner ('14) in his book on the germ-cell cycle of animals, germinal-epithelium theories of germ-cell origin have little evidence in their favor, since no one has "actually observed a transformation of peritoneal or mesoblast cells into germ cells." "On the other hand there is an abundance of proof that these cells (primordial germ cells) migrate from some distance into the position of the sex glands." ('14, p. 99).

Hegner's own work on Chrysomelid beetles ('09a) brought evidence of a migra-

tory process. In these insects the primordial germ cells were segregated at the posterior end of the egg at the time when the blastoderm was formed. The blastoderm was never completed beneath them, but a canal which formed in this region persisted, and through this at a later embryonic stage the germ cells migrated by means of amoeboid movements:

> As soon as the germ cells of *Calligrapha* have passed through the pole-cell canal, they lose their pronounced, pseudopodia-like processes and become nearly spherical; nevertheless they (still) undergo a decided change in position. They move away from the inner end of the pole-cell canal, and creep along between the yolk and the germ-band. Thus two groups are formed near the developing coelomic sacs; each group probably contains an equal number of cells. . . . . From this stage on, the germ cells are not very active; they move closer to one another to form the compact germ glands. I was unable to determine whether the later movements of the germ cells were due to an active migration or to the tension created by the growth of the surrounding tissues; the latter seems more probable ('09a, p. 280).

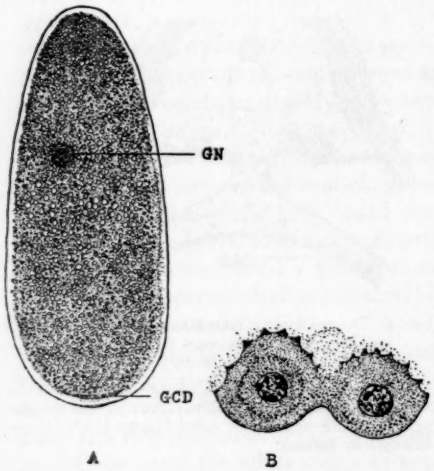

FIG. 7. A—LONGITUDINAL SECTION THROUGH THE EGG OF CALLIGRAPHA BIGSBYANA FOUR HOURS AFTER DEPOSITION, SHOWING GERM-CELL DISC AT THE POLE OF THE EGG. B—TWO TYPICAL GERM CELLS

GCD—germ-cell disc. *GN*—germ nuclei fusing. After Hegner in *The Germ-Cell Cycle in Animals*.

In paedogenetic reproduction in the fly, *Miastor americana*, Hegner ('12) followed the history of the germ cells from one generation to the next:—in the division from four to eight cells three of the four nuclei of the four-cell stage divide by mitosis in the usual manner, but one cell in division gives to its daughter cells only one half the usual chromatin. One of these reduced chromatin cells is always found at the end of the blastula in the pole-plasm. The single primordial germ cell divides three times giving eight germ cells. A resting period sets in, and these cells are passively carried to a point near the tail fold of the embryo. The eight oögonia separate into two groups of four each, and the ovary forms around them. Such a history looks like Weismannian continuity of germ-plasm. (See Fig. 2).

The work of Swift

Three papers by Swift, appearing in consecutive years ('14, '15, '16), described his researches on the germ cells of the chick. The first noticeable attributes of primordial germ cells recorded by Swift were their size and shape, both being conspicuously different from those of surrounding cells. The germ-cell nuclei were also definitely characteristic, but the most important criterion, according to Swift, was the large, ever-present attraction sphere. Rubaschkin ('08) and von Berenberg-Gossler ('12) stressed this criterion earlier. Swift gave little attention to mitochondrial elements, since he considered them not at all characteristic and quite like the mitochondria of somatic cells. According to him the germ cells arise in a region anterior and antero-lateral to the embryo at the margin of the area pellucida. Owing to the late appearance of mesoderm in this region, these cells were seen first between the entoderm and the ectoderm. They seemed to possess a migratory power of their own and entered

the mesoderm and later the blood vessels. Swift believes the primordial germ cells of his observation identical with the "entodermal wander-cells" described by Dantschakoff ('08), but he disagrees with her in that he observed no degeneration, which she believed eliminated all primordial germ cells so that they took no part whatsoever in gonad formation. Swift concluded from his observations that practically all primordial germ cells do persist, and are carried in the blood stream

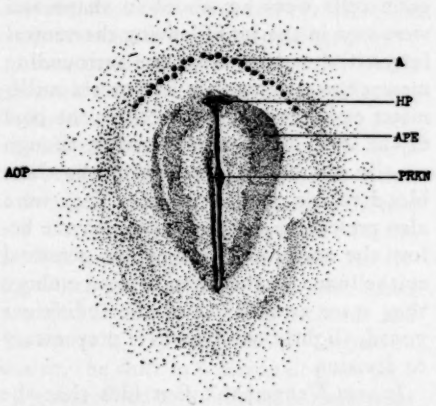

FIG. 8. SURFACE VIEW OF A PRIMITIVE-STREAK STAGE OF A CHICK EMBRYO, VIEWED BY TRANSMITTED LIGHT, SHOWING THE POINT AT WHICH THE PRIMORDIAL GERM CELLS ARISE

A—region at which the primordial germ cells arise. *HP*—head process. *PRKN*—primitive knot. *AOP*—area opaca. *APE*—area pellucida. After Swift in *Amer. Jour. Anat.*

to all parts of the embryo and vascular area. (Compare Fig. 3.) This general distribution maintains until the embryo has reached the stage of about twenty somites. From the twenty-second to the twenty-ninth-somite stages these cells gradually take up their residence in the splanchnic mesoderm and the coelomic epithelium. When the gonad proper begins to be formed about the sixth or seventh day of incubation, they pass into that organ, the extra-germinal tissues arising as proliferated cords from the epithelium.

The work of Vanneman on the armadillo

In 1917 Vanneman, studying the armadillo, *Tatusia novemcincta*, was able to distinguish germ cells, and experienced no difficulty in identifying them from the earliest stages. Size and form were remarkably constant throughout development. The primordial germ cell is described by her as large, about twice the size of an ordinary erythrocyte, and, in contrast to neighboring cells, light in staining reaction. These cells were typically spherical, but at times, and especially in early stages, the shape was very suggestive of amoeboid movement. The cell outline was always very definite, and this was taken as one of the most dependable criteria of germ cells. Concerning the criteria used by other investigators for distinguishing germ cells, Vanneman has little to say except that neither was the presence of yolk substance sufficiently constant to be used in the identification nor the attraction sphere of Swift frequently enough apparent to be used as a criterion.

In the armadillo, as worked out by Patterson ('13), the usual cleavage stages take place with the formation of a typical mammalian blastocyst, consisting of one trophoblastic layer and an inner cell-mass of embryonic cells. A process of differentiation sets in through the migration of the entodermal mother-cells from among the ectodermal cells. These cells directly, or after division, migrate to the under surface of the cell-mass and presently become transformed into a continuous layer which splits from the ectoderm. The embryonic ectoderm now rounds up into a spherical mass which withdraws from the trophoblast, and pushes into the vesicle cavity, becoming included in a

layer of entoderm. Through the process of vacuolization, the ectoderm sphere now becomes a vesicle. After this stage the primary buds first appear from the thickened areas which have arisen on the opposite sides of the ectodermic vesicle through a shifting of cells. The primary buds show no signs of embryonic primordia, but each directly gives rise to two secondary diverticula, forming four buds which are soon extended, and begin to show the beginnings of four primitive streaks destined to become the quadruplets. Each embryo derives its ectoderm from a part of the lateral plate, while the entoderm arises from the primitive entodermal sac. From such a developmental beginning Vanneman considered it possible that the germ cells of all four embryos might have a common origin.

Early germ cells were located by Vanneman between the ectoderm and entoderm at the time when the primary buds and the ectodermic vesicle were in the process of formation. They were exceedingly few in number, a fact also recorded by Swift ('14) for the chick in embryos earlier than the primitive-streak stage. The cytological resemblance of these early cells to adjacent entodermal cells, together with the presence of cells actively dividing, suggested the possibility that at this point for the first time germ cells were being proliferated from segregated cells, which up to this time had not been distinguished from surrounding tissues. But it was not until the secondary bud-stage was reached that the germ cells were found in any numbers. Vanneman indicates that such an origin for germ cells is, in general, similar to Swift's findings as regards place, method, and time:

> The entoderm of the mammalian blastocyst is analogous to the yolk sac entoderm of the lower vertebrates. It is not unreasonable to suppose that in the armadillo the germ cells arise during the secondary bud state in the embryonic areas through the influence of the ectodermic vesicle upon the blastocyst-entoderm at the point where the two layers come into contact. Observation seems to confirm this. That the germ cells have not arisen in numbers any earlier may be due to the fact that there exists previous to the early primitive streak stages no incident, such as the coming in contact of ectodermic and entodermic layers, to favor the proliferation of germ cells. ('17, p. 335).

At the time when the embryo had attained four millimeters length and acquired a pronounced cervical bend, the germ cells were amoeboid in shape and were seen in the act of leaving the ventral interstitial wall to enter the surrounding mesenchyme tissue. In five to six millimeter embryos they appeared at the base of the well-developed mesentery, though usually not below the level of the three blood vessels of that region. They were also present in the loose mesenchyme below the aorta, en route to the germinal epithelium. In the ten millimeter embryo they were established in the indifferent gonad, slightly enlarged as if preparatory to division.

It was Vanneman's first idea that the germ cells of the four embryos of one vesicle might have a common origin as the early development suggested, but no evidence supporting such an origin was found, at least in the sense of having arisen from "a pre-localized region of the early blastocyst."

In the catfish, *Amiurus nebulosus*, Bachman ('14) traced the migration of germ cells beginning with embryos measuring 3.2 millimeters. Germ cells were distinct from all other cells at the 3.2-millimeter stage and thereafter. At this time they were present in the lateral plate of the mesoderm, from which they finally found their way to the germ-gland anlagen. Bachman reported no transformation of peritoneal cells and considered division the sole means of germ-cell multiplication.

Jordon ('17) favors early segregation and persistence of germ cells, and takes issue with von Berenberg-Gossler ('12, '14), who studied large cells in the ectoderm and mesoderm outside the genital region of reptiles and birds, and denied their germinal character, explaining them as participants in mesenchyme formation. Jordon says that such results are "unique and do not seem capable of being brought into harmony with results in any other form thus far studied—", and again, "this interpretation is more or less plausible but cannot be said to be wholly satisfactory."

From an extensive investigation of the germ-cell history in the brook lamprey, *Entosphenus wilderi* (Gage) Okkelberg ('21) was led to the belief that definitive germ cells take their origin from no other source than the primordial germ cells, and that the germ cells take no part in the formation of somatic structures. He distinguished germ cells by their size, structure, and location, and like Richards and Thompson ('21) considered migration passive, the shift in position of germ cells being accredited to a shifting of the tissues surrounding the cells. These cells were first identified in the brook lamprey when the mesoderm separated from the entoderm, before the germ layers were definitely established. During the early period of their history the germ cells were observed to shift from a lateral position in the mesoderm to a median position. No division of germ cells took place until the larvae were about 20 mm. in length. By this time the large germ cells had lost the yolk granules which characterized them earlier. After each mitotic division the two daughter cells separated slightly but remained in close proximity, forming cell nests. Peritoneal cells migrated into these nests and formed follicle cells. As sex differentiation approached the nests of cells gradually became constricted off, forming a definite germ gland.

The work of Swingle

Swingle ('21, '26) distinguished primordial germ cells in the entoderm of the bullfrog embryo, and traced them to the formation of the sex gland, and up to the time of metamorphosis. He located the earliest recognizable germ cells as a median ridge of yolk-laden cells just dorsal to the roof of the archenteron, ventral to the aorta, and separating the two mesodermal plates from each other. In embryos of eight millimeters length the germ-cell ridge had become separated from the underlying entoderm forming the roof of the archenteron. Swingle believes that migration is by movement of surrounding tissues but also that there is an active migration of the germinal elements themselves. As development progressed this median ridge split longitudinally, and the cells of the two halves moved laterally on either side to form two independent ridges invested with peritoneum. At this stage the total embryo length was about nine millimeters. The two germinal

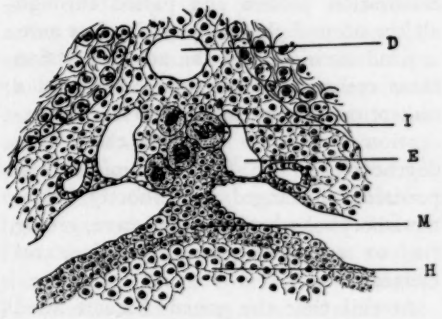

FIG. 9. TRANSVERSE SECTION THROUGH THE GERM-CELL REGION OF AN EIGHT-MILLIMETER LARVA

I—germ cells. *M*—mesentery. *D*—aorta. *H*—entoderm cells. *E*—cardinal veins. After Swingle in *Jour. Exper. Zool.*

ridges next projected into the coelomic cavity and enlarged markedly, the number of cells being increased by cell division. When the tadpole had attained a length of thirty millimeters, the gonads were definitely formed, appearing as hollow sacs surrounded by a single layer of peritoneum and made up of one or two layers of germ cells.

All increase in the number of germ cells up to the forty millimeter length was, beyond question, Swingle thinks, by mitotic activity of the pre-existing (primordial) sexual elements. At the 40 mm. stage the germ cells seemed to enter a maturation process and passed through all the normal phases up to the first maturation division. In the act of division these spermatocytes disintegrated, and a resorption process set in. With the exception of a very few, all these cells degenerated. The few remaining cells persisted unchanged, and shortly before metamorphosis became very active, giving rise to a second generation of sexual elements.

At this time the gonads became filled with small cells which from their size, nuclear appearance, staining reaction, etc., seemed intermediate between mesothelial cells and true germ cells. The later history of these cells showed them to be germ cells, and the author considered them small germ-cell descendants of the primordial sexual elements, but he hesitates to deny the possibility of their origin from the peritoneum.

Swingle is inclined to agree with Hegner ('14) regarding the germ track in vertebrates, but he is not ready to believe that germinal-epithelium theories have so little in their favor. He says:

> Though regarding himself as an entodermist, and taking the point of view that the "*Keimbahn*" is probably continuous in vertebrates and that there is no actual transformation of mesothelial elements into sex cells, the writer admits that conditions are such in the bullfrog that it is impossible to state positively that the primordial germ cells of the bullfrog tadpole do give rise to the definitive sex cells of the adult frog. ('21, p. 289–290).

In this connection Swingle points out that the only adequate method of attack is by experimental procedure. Morphological methods are insufficient to determine whether or not a germ cell is a transformed epithelial element or a small descendant of the primordial line.

The work of Richards and Thompson

A paper by Richards and Thompson ('21) had as its special aim the definite identification of the primordial sex cells and the determination of the germinal path in *Fundulus* embryos. These authors experienced no difficulty in recognizing primordial germ cells, for they found them to maintain distinctive characteristics throughout the migration period. Primordial sex cells varied in diameter from nine to 128 micra, and, contrasted with other cells, were spherical or ovoid with very definite cell-outlines. The nuclei seemed to conform to the general shape of the cells. Richards and Thompson observed in *Fundulus* no peculiar invagination of the nuclear membrane such as was reported by Dobbs ('10). An unusually large centrosome plainly visible in the cytoplasm was always characteristic of these cells. In older embryos germ cells were recognized by their size.

Positive identification of primordial sex cells was made in a twenty-four-day embryo in which they were seen in sac-like anlagen of the reproductive organs dorsal and slightly lateral to the hind gut, numerically inferior to the cells surrounding them. From this stage their path was followed backward through all intermediate phases of migration, until they were no longer evident. At forty-six to

fifty hours the position of the germ cells was striking, being widely distributed throughout the embryo, a fact also recorded by a number of other observers.

The authors considered that observation of these early embryos revealed several important facts: the primordial germ cells were as truly characteristic and as easily recognized as any found in the germ glands of later stages; they were located in the posterior half of the embryo, becoming gradually more numerous as the anterior part of this region was approached; laterally they ranged from the extra-embryonic tissues to within the lateral mesoderm and the edge of the developing gut. In general the progress along the "germinal path" was directly proportional to the developmental stage of the embryo.

They believe that the early distribution and migration of sex cells is best explained by the forces of growth, that is, the streaming of organ-forming tissues which contribute materials to different parts of the embryo. They consider of great significance the fact that no sex cells were found in that part of the embryo which develops from the head fold. The germinal path led from the peripheral entoderm into the border of the undifferentiated entodermal cell mass. By the time the gut was formed these cells were lateral to it, and they all eventually became located in the splanchnic mesoderm of this region. From these they migrated dorsal to the gut to a region ventral to the Wolffian ducts. Here they became surrounded by peritoneal cells which formed the somatic portion of the gonad. From this position the germ-gland anlagen were shifted back to their final position dorsal to the gut. Such is the story of the primordial germ cells according to these authors, and in conclusion they say "that evidence derived from this study of *Fundulus* is in absolute harmony with the theory of early segregation of primordial germ cells." ('12, p. 339).

The work of Cowperthwaite

An interesting approach to the problem of the origin of definitive germ cells was made by Cowperthwaite ('25) in which the occurrence of meiotic phases was considered the criterion of a definitive oocyte.

The first series of ovaries studied was taken from a group of rats ranging in age from newly-born to eight days. This group was selected because the later phases of meiosis are known to occur in oocytes during this period. A second series was taken every ten days from the tenth day after birth to the ninetieth day, thus including ovaries from individuals at the time of weaning, puberty, and sexual maturity. A third series was secured from mated rats. The birth date of the first litter was recorded, and the litter was taken from the mother. Using Donaldson's ('15) information that ovulation occurs in the rat twenty to forty-eight hours after parturition, the females were allowed to mate again at once. The second litter was removed immediately as before. This was done in order to avoid the lactation inhibition of oestrous activity, since it was desired that females undergo normal oestrus in the presence of the male. Ovaries were preserved from females at the time of the second parturition and on the first, second, third, fourth, fifth, and sixth days thereafter. In this way it was hoped to cover the entire oestrous cycle.

Early meiotic phases occur in embryonic ovaries, and at the time of birth the thick threads of the pachytene stage appear. Cowperthwaite's studies began at this point. By the end of the fourth day postpartum, meiosis had been completed and no transitional stages were to be found

"between the undifferentiated germinal epithelial cells and the post-meiotic germ cells." A study of size differences and nuclear condition of small as compared to large oocytes led to the conclusion that the smaller follicles represent a retarded growth condition and that they are not derived from a new germ-cell formation as many have supposed. This conclusion was reached by the author chiefly because of a failure to find "fresh meiotic phenomena in the germinal epithelium either at this age or at any succeeding period in the series of ovaries studied." ('25, p. 79).

In the rat a new oestrous cycle normally occurs directly after a parturition. Ovulation, which takes place at the height of the cycle, may be expected to occur from twenty to forty-eight hours after the birth of a litter. With this in mind Cowperthwaite made observations on a series of ovaries which covered the entire cycle. Contrary to the findings of Allen ('22, '23) no evidence was found throughout the series that new germ cells are proliferated periodically from the germinal peritoneum. The only possible evidence of periodicity was found in the observation that more cells were seen enlarging *in situ* in the ovaries preserved near the time of parturition, and on the fifth day thereafter. Since each of these periods corresponds to the beginning of a new oestrous cycle, and resting cells would, therefore, be entering a growth period preparatory to ovulation at the height of the cycle, Cowperthwaite considered this periodicity adequately accounted for. In view of the significance of meiotic phases in the history of germ cells, she concluded that oogenesis is not continued during pre- and post-pubertal life, and new germ cells are not proliferated periodically from the epithelium.

Duesberg in 1908 made a study of spermatogenesis in the white rat, but, for some reason, found no indication of synapsis or other meiotic phases.

The work of Swezy

Swezy ('29a), on the other hand, records observations on maturation in the male rat of a distinct and prolonged synapsis which occurred just before synizesis.

In the female rat ('29b) Swezy found ova arising by proliferations from the germinal epithelium, all the cells of which she believes are potential ova. According to Swezy this proliferation begins with the differentiation of the gonad and may last as long as 369 days after birth. The embryonic ovary is filled with ova which undergo typical maturation phases. Meiosis continues until five days after parturition. But the ova, Swezy believed, degenerate, since none was found in the ovary of the twenty-day rat. After the fifth day no typical maturation phases were present. Swezy says: "With the degeneration of the embryonic ova the ovary takes on adult structure. The ovary of the adult female rat shows the typical phases, indicating that this is the primitive type, with the modified form an acquired characteristic." Swezy is particularly interested in chromosome numbers in mixed rat strains.

Two recent papers by Swezy and Evans ('29a, '29b) report studies on maturation of human embryonic ova and of ovogenesis in several mammals, the guinea pig, the cat, the dog. In human embryos of the third month early maturation phases of the ova were found. These phases consisted of typical formation of leptonema, synizesis, pachynema, and diplonema. Prochromosomes, similar to those of insects, were found in leptonema which later resolved into leptotene threads, a phenomenon hitherto not observed in mammals. In embryos of five and one-

half months all these prochromosomes had disappeared. Swezy and Evans believe that these embryonic germ cells all disappear before adult life is reached, and that the ova developed during adult life do not pass through these phases preliminary to maturation.

From observations on the guinea pig, cat and dog, these authors conclude that ovogenesis occurs throughout adult life as a rhythmical process, and that during the life-time of the individual, literally thousands of ova are produced *de novo*. Such a conclusion recalls the results obtained by Allen ('22, '23) in the mouse. In the guinea pig, cat, and dog the rhythmical proliferation of new cells from the germinal epithelium coincided with the oestrous rhythm. Though it is difficult to make this correlation in man because of a lack of knowledge of the cycle, Swezy and Evans believe that ultimately such a coincidence will be found for man as well as other mammals.

The conclusions arrived at here substantiate the work of Swezy, as is indicated by the following: (Exp. Biol. Med., 27, p. 11).

> New sex cells are produced by proliferations from the germinal epithelium in the form of invaginations and ingrowths of epithelial cords. These become separated from the germinal epithelium, pass through the tunica albuginea and form a more or less continuous layer underneath the tunica. From one to many cells in each group may develop into ova, the remaining forming the follicle cells.
>
> Contrary to the concept involved in the germ plasm theory, the mammalian ova (excepting those that mature and are fertilized) have a shorter life-span than any other group of cells in the body outside of the reproductive tract.

Willier ('26) identified primordial germ cells outside the chick embryo (extra-embryonic) and designed experiments to determine whether they were essential for gonad development, and whether the gonad would develop any germ cells in the absence of the primordial germ cells. The blastoderm of chick embryos incubated nineteen hours was removed and the area pellucida isolated so as to be free of all primordial germ cells. The isolated area pellucida was implanted in a host embryo of nine hours incubation. After nine days, histological examination showed the anterior part of the embryo well developed: large brain vesicles partially surrounded by cartilage, medulla, ganglia, pigment layer of the eye, bone, gut, oral cavity, hypophysis, muscles, etc., but the more posterior parts of the embryo were absent entirely or very poorly developed. The entire absence of a gonad was striking.

Richards, Hulpieu, and Goldsmith also in 1926 investigated the history of germ cells in a series of chick embryos from the beginning of incubation to 180 days after hatching. The early development as described by these authors is entirely in accord with that described by Swift ('14, '15, '16). The primordial germ cells arise in the extra-embryonic region and are carried in the blood stream to the gonadial ridge. In the male from the eleventh day of incubation, division of sex cells took place actively with no signs of degeneration, although their history was followed for seventy-five days. An even more complete series was available in the female, and no transformations of peritoneal cells into germ cells were observed. The history of developing ova is purely one of growth, division, and preparation for maturation. These authors are confident that the definitive ova are all traceable to early-segregated germ cells without degeneration and without contributory proliferations from the germinal epithelium. Small cells from the peritoneum go into the formation of the follicles but not of the definitive ova.

Woods ('25, '29) made observations on

living and sectioned material covering the various stages in the life-cycle of *Spaerium striatinum*, the viviparous bivalve, and concluded that the germ-cell history was traceable from the fertilized egg to sexual maturity. He divided the cycle into six general periods with fairly definite limits. Primordial germ cells of characteristic structure appeared just before gastrulation. One large germ cell appeared in the mesoderm mass on either side of the blastocoele, and of these, according to Woods, all germ cells are direct descendants. The ectomesoblasts, he thinks, contribute nothing to the formation of germ cells. Metamorphoses of somatic cells into germ cells are not observed in the material studied. During maturation certain granules appeared in the cytoplasm of the ovum. During cleavage these granules segregated into those cells which give rise to germ cells. Woods is particularly interested in these granules, their origin, nature and significance.

From an investigation of germ-cell history in the teleost, *Cottus bairdii*, Giraid, Hann ('27) concluded that definitive germ cells in both sexes have their origin only in primordial sex cells, since no transition from somatic cells to germ cells was observed at any stage. Hann thinks the original source of primary germ cells is the entodermal giant cells first found before the gut was formed and later along the ventral and lateral margins of the gut. Some of these cells passed through the lateral mesoderm to a position dorsal to the gut, from which they were shifted to the gonadial region. This interpretation is entirely in accord with that of Richards and Thompson ('21) in their observations on *Fundulus* embryos.

Sex could be distinguished first at fifty-two days, in the female by early maturation stages and in the male by the presence of the sperm duct. A part of the oocytes formed during the first season matures for the first spawning, which takes place at the age of two years. The remainder form a reserve supply, which is increased each year by dormant oogonia become active. In the male spermatogonia lying dormant in the cysts during maturation give rise to sperm at the next season.

The work of Humphrey

Humphrey in 1925 began a study of primordial germ cells in Urodeles. In the first report, based entirely upon morphological studies, the author states his conclusion that the primordial germ cells of the Urodeles are mesodermal in position from the time the mesoderm and the entoderm become separate germ layers. With this interpretation previous workers on Urodele germ cells, particularly Dustin ('07) and Allen ('11), are in agreement.

The early position of the primordial germ cells is described by Humphrey in *Hemidactylium* and other Amphibia. He found that these cells lie in the mesoderm just lateral to the somite. At this stage they showed no nuclear distinguishing features, but in size and in abundance of yolk, they were equal to the germ cells of older embryos. Later these cells were seen crowded medially against the entoderm. At this time nuclear peculiarities marking them as germ cells were distinguishable. During the further growth-shiftings of the mesoderm, these cells were carried medially and came to lie in the genital ridges on each side of the gut.

Humphrey ('27, '28, '29) next carried his studies into experimental work on the germ cells of *Amblystoma*, approaching the problem from a somewhat different angle. Mesodermal cells and large cells thought to be primordial germ cells were transplanted to the lateral body wall of the embryo. In five out of seven cases these transplanted primordial germ cells gave

rise to a gonad on the site. The author concluded that "primordial germ cells may survive, differentiate, and produce an ectopic gonad when transplanted before they become morphologically recognizable." ('27b, p. 40).

Part of the experimental work ('27a) consisted in the extirpation of the primordial germ cells of *Amblystoma* and its effect upon the developing gonad. Here Humphrey found that complete extirpation of the area of mesoderm in which the primordial germ cells are to be recognized results in the absence of the gonad.

A similar conclusion ('29) resulted from a study of sex differentiation following orthotopic implantation. The author considers that the area of mesoderm of *Amblystoma* in which germ cells are recognized may be regarded as the preprimordium of the gonad, since implantation of this area results in the development of a gonad. The area extends from the level of the eight or ninth somite to that of the sixteenth or seventeenth, and is intermediate between the axial and lateral divisions of the mesoderm. Humphrey believes that the primordial germ cells are mesodermal in derivation and must be located in the mesoderm from the time the germ layers are first separated.

The work of Goldsmith

Goldsmith ('28) in tracing the history of the procreation cells in the domestic fowl found large size, spherical shape, the presence of an attraction sphere, and clear staining reaction of the nucleus reliable criteria for identifying germ cells. Primordial germ cells were first seen in the embryo during the primitive streak stage at the outer edge of the proamnion anterior and antero-lateral to the head fold. Before the mesoderm formed they were found in the space between the entoderm and the ectoderm. But later as the mesoderm grew into space the primordial germ cells became incorporated in it and by their own movement found their way into the blood vessels. Up to the thirty-three hour stage of incubation they were found only in extra-embryonic tissues. Goldsmith figures primordial germ cells within the blood vessels of the splanchnopleure of a twenty-four hour embryo, and at various locations in later stages. He points out in this connection the correspondence between his observations and the findings described by both Dantschkoff ('08) and Swift ('14).

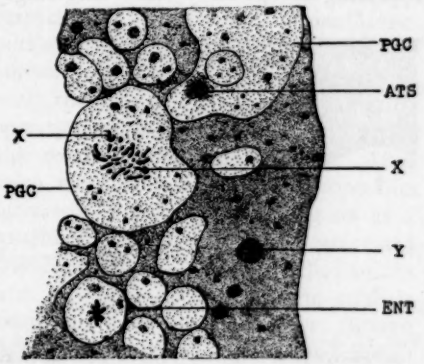

FIG. 10. SECTION THROUGH THE REGION ANTERIOR TO THE HEAD FOLD, SHOWING THE POSSIBLE PRIMORDIAL GERM CELLS STILL EMBEDDED IN THE ENTODERM. SHOWS GREAT DIFFERENCE IN SIZE BETWEEN THE PRIMORDIAL GERM CELLS AND SOMATIC CELLS

ENT—entoderm cells. *X*—sex chromosome. *PGC*—primordial germ cell. *Y*—yolk. *ATS*—attraction sphere. After Goldsmith in *Jour. Morph. and Physiol.*

When the embryonic and extra-embryonic blood systems joined, the primordial germ cells were found in the embryo itself (at thirty-three-hours incubation). Wide distribution of the germ cells throughout the embryo was evident until about the forty-hour stage, when they become more numerous at the site of the gonad, though at this stage many were still present in the blood stream. They gradually took

up residence in the developing germinal epithelium, and by the sixth or seventh days sex could be determined reasonably and accurately, though for absolute certainty the chromosomal complex alone is reliable. In the male cells two large V-shaped chromosomes were present while the female cells showed only one.

Goldsmith observed no "wide-spread degeneration of the primordial germ cells of either sex" and places confidence in the belief that these primordial germ cells appearing in the early embryonic stages

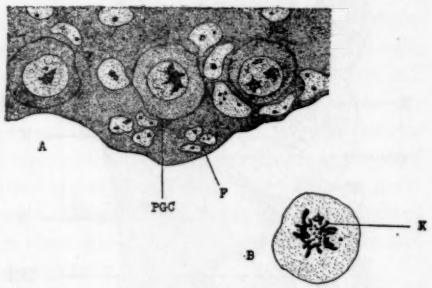

FIG. 11. A—A SECTION THROUGH THE OVARY OF A SEVEN-DAY EMBRYO SHOWING THE PRIMORDIAL GERM CELLS PLACED IN THE GERMINAL EPITHELIUM. THE THICKNESS OF THE EPITHELIUM IS INDICATIVE OF A FEMALE. B—A SINGLE GERM CELL SHOWING METAPHASE PLATE

F—follicle cell. *PGC*—primordial germ cell. *X*—sex chromosome. After Goldsmith in *Jour. Morph. and Physiol.*

maintain their identity, and "continue through to form the definitive germ plasm."

Stromsten ('29) has studied the history of germ cells in the goldfish. His observations favor the theory that the germ cells migrate through the dorsal mesentery to their destination beneath the floor of the swim bladder.

THE BEARING OF REGENERATION ON THE ORIGIN OF THE GERM CELLS

Aside from the purely cytological aspect, an interesting approach to the problem of the definitive germ cells has been made from an entirely different standpoint, that of regeneration of the gonad following removal. Swingle bordered on this idea in his 1921 paper on the germ cells of Anurans, when he said:

> . . . . Certainly this is the more probable view [that primordial germ cells of the tadpole alone give rise to the definitive sex cells of the adult frog], though the burden of proof rests with those of us who hold that the *Keimbahn* is continuous. . . . . It would seem from this that the crux of the whole problem is to determine whether or not germ cells can develop in an organism after the primordial germ cells have been destroyed. If they do develop, then the doubtful question of the transformation of mesothelial cells into germ cells is settled in favor of the mesodermists, but if they do not develop, and the gonad is sterile and remains so up to the period of sexual maturity, then the decision is in favor of the entodermists ('21, p. 290).

The work of Willier ('26) previously mentioned, is interesting in this connection. It brings evidence that in the chick no germ cells develop in the absence of primordial germ cells. Where the areae pellucidae were isolated free of all germ cells, the entire absence of the gonad was striking.

Regeneration in Coelenterates has been considered dependent upon the presence of latent germ cells such as Weismann ('93) found in the ectoderm of Hydromedusae. Weismann took the position that regeneration is due to the presence of germ plasm, since that is the only substance which can give rise to all parts of the body. Montgomery ('06) and Hegner ('14) accept the germ-cell explanation, believing that regeneration in Coelenterates is due to widely distributed germ cells. Hargitt ('16, '17, '18, '19), however, found no direct evidence in favor of this view. He concluded that "the great body of facts concerning regeneration in many phyla contradict such an interpretation. Especially do the observations upon regeneration from iso-

lated cells of hydroids disprove the germ-plasm theory." Hargitt, confirming Wilson ('13) explains regeneration thus: "they [isolated cells] become despecialized into potentially embryonic cells and probably from this change have acquired their regenerative capacities."

Morgan ('01), after discussing a considerable number of theories of regeneration, also rejects the germ-plasm theory completely, finding many facts of regeneration which are incompatible with such an explanation.

Castle and Phillips ('11, '13) removed ovaries from a series of seventy-four guinea pigs and seventeen rabbits. The tube so far as possible was left intact. "Ten animals showed regenerated ovaries and three had young. Forty-two showed at post-mortem complete atrophy of the genital tract and absence of ovarian tissue." ('11, p. 8). In a later paper ('13) these authors offer a summary of their experiments on 141 female guinea pigs:

"In eleven cases ovarian tissue was regenerated at the original ovarian site and in three of these cases young were produced having the genetic characteristics of the mother."

The work of Davenport

In connection with studies dealing with fecundity and ovarian transplantation, Davenport ('25) performed a series of ovariotomies in mice. As the experiments progressed it became evident that ovarian tissue was again present at the site of the operation. This discovery led to a study of regeneration, and Davenport was interested in answering the following questions:

"Under what conditions does regeneration occur and what conditions inhibit it? What is the site of the regeneration? Are young produced from eggs derived from the regenerated ovary?" ('25, p. 1).

In the first series, consisting of thirty-one operated mice from which thirty-eight ovaries were removed, both the capsule containing the ovary and the coiled Fallopian tube were excised. In the second series, comprising ninety operations, the capsule was "slit open opposite to the stalk and folded back, exposing the ovary. The ovary was then removed with as much of its short stalk as feasible." ('25, p. 2).

Sixty-four per cent of the operations were followed by more or less complete reappearance of the ovary. From Davenport's analysis it appears that the proportion of regeneration increased directly with the interval elapsing between the operation and the examination, from about nine weeks to twenty-five weeks. After seven months, however, the proportion decreased, and Davenport suggests as a possible explanation that the regenerated ovaries might have been absorbed in the later months. The age of the animals seemed to have no clear effect, though Davenport observed that regeneration rates for mice between nine and ten weeks of age were relatively low, while some at four weeks gave as high as eighty-three per cent. Ages ranged from one to four months.

The ovary usually regenerated at the site of the one removed, though in some cases the regenerated ovary was located caudad to the tube, seeming to indicate that regeneration may take place as much as five or six millimeters distant from the operated site. Usually no embryos were found in the horn of the uterus on the operated side, but corpora lutea were frequently found in regenerated ovaries, and in some few cases embryos were found in the horn of the operated side.

In fourteen cases no trace of the capsule could be found at autopsy, and yet ovarian tissue was present. Davenport considered this strong evidence that regenera-

tion of the ovary may take place from tissue proximal to or lateral to the stalk. He also considered that this observation indicated that the old ovary had been completely removed and the new formation was not merely an enlargement of a fragment of the old ovary that had been left in place. No histological verification of this claim was attempted; macroscopic examination of masses of tissue at or near the site of the operation was the criterion of regeneration. According to the writer's observations, which will be described subsequently, the absence of a capsule at autopsy in adult rats is no indication that complete ovariotomy was accomplished.

The presentation by Hargitt of his observations on germ-cell history in the male rat at the Kansas City session of the American Association for the Advancement of Science in 1925 was followed by a discussion of the evidence for germ-cell continuity in general. At this time Davenport suggested that even if germ cells do arise from soma cells, we are still dealing with a continuity of chromosomes, since the chromosomal complex of somatic cells is descended directly from germ cells; and that this "saves the day" for continuity. He pointed out that it is the cytoplasm of the cells which takes part in differentiation into specialized body cells. In the course of the general discussion the idea was advanced that the interaction between the nucleus and the cytoplasm of a cell is sufficient to render such a conclusion questionable.

The work of Parkes and his associates

Indirect evidence for proliferations from the germinal epithelium comes from studies by Parkes ('26, '27, a, b, c,) and Brambell, Parkes and Fielding ('27 a, b, '28) of the effects of irradiation in the mouse, though no very definite claim is made by these authors that the cells which were proliferated after partial or complete sterilization were germ cells.

Parkes found that when the young female is irradiated at three weeks of age (Part I) the result is complete degeneration of ova, granulosa cells, theca interna, where it has differentiated, and that the ovary subsequently comes to consist almost entirely of extra-follicular tissue, that is, of proliferations from the epithelium. In animals irradiated at birth (Part II) the course of events is similar to that found in those irradiated at three weeks old, but "in some few instances the proliferation from the epithelium becomes extremely luteal-like." An interesting age difference was apparent when adults were irradiated, namely, that while irradiation of the adult obliterated all follicles, as in young animals, no post-irradiation proliferation of tissue from the germinal epithelium took place. Parkes was interested here not in demonstrating that these proliferations did not consist of germ cells, but in the occurrence of the oestrous cycle after X-ray sterilization and subsequent follicular degeneration, showing that neither the follicle nor the corpus luteum is necessary for the maintenance of the oestrous cycle. However, from Parkes' description of the post-radiation proliferations, one concludes that they consisted entirely of extra-follicular tissue.

The work of Brambell, Parkes, and Fielding was similar in procedure to that of Parkes. Simultaneously with the degeneration of the follicles, the inter-follicular tissue atrophied and the germinal epithelium proliferated epithelial cords. In the adult animals the ovaries were composed almost entirely of this first proliferation. In many cases a second proliferation from the germinal epithelium followed. These resembled the so-called spermatic cords described by some authors in the ovaries of rabbits and free-martin

cattle, or structures called by many "anovular follicles." That these authors consider the possibility that some cells of these proliferations may be ovular follicles is indicated by the statement that the "post-irradiation proliferations might correspond to the definitive proliferations of the normal ovary described by de Winiwarter and Sainmont" ('09). ('27 a, p. 111.)

The same age differences as reported by Parkes were observed by these authors ('28). Irradiation of the adult during pregnancy produced a rapid degeneration of oocytes and larger follicles, but none of these animals showed any signs of proliferation and ingrowth from the germinal epithelium such as was described in animals irradiated before puberty. Also when adult animals were irradiated during lactation the germinal epithelium remained thin and inactive.

One series of experiments was initiated with a view to ascertaining whether after sterilization and unilateral ovariotomy at three weeks old, the remaining (sterilized) ovary hypertrophies as is true in normal unilateral ovariotomy. While the results are insufficient for very definite conclusions, there seemed to be a true compensatory hypertrophy of the ovary. No indication is given as to the source of the cells or whether the authors considered the proliferated tissue germinal.

In 1926 Parkes and Bellerby conducted a series of ovariotomies on mice in connection with work on injection of the oestrus-producing hormone. These authors state that their findings on regeneration confirm those of Davenport, the criterion of regeneration being the spontaneous reappearance of oestrous phenomena. They considered the possibility of regeneration so great as to prejudice the hormone-injection tests which were the original purpose of their experiments.

Later ('27) a paper appeared by Parkes, Fielding, and Brambell on regeneration after double ovariotomy, continuing the method of Parkes and Bellerby. The oestrous cycle in eleven animals ceased after double ovariotomy for a longer period than could be accounted for by an unusually long dioestrous interval, and since only a very small amount of ovarian tissue is required to maintain oestrus, this complete cessation was considered by the authors to indicate removal of ovarian tissue. The extirpated ovaries were fixed and sectioned to give histological evidence of complete removal.

Vaginal changes characteristic of the oestrous cycle recommenced in all eleven animals. In eight of these cases ovarian tissue was demonstrated histologically. One was not available for observation, and the remaining two failed to show any regenerated tissue. However, the authors consider that since oestrous phenomena recommenced some small bit of ovarian tissue must have been present which was overlooked in dissection. In four animals the oestrous cycle did not return and no regenerated tissue could be detected from a study of serial sections of the ovarian region. The total number of animals involved was 121, each doubly ovariotomized. The above described operations consisted of removal of ovaries, capsules, and portions of the tubes.

Tamura ('27), in a study of implantation of ovarian grafts in the male mouse, found that the success of the grafted tissue depended primarily upon its vascularization and secondarily upon the activity of the germinal epithelium of the graft itself; and that about sixteen days after transplantation a new proliferation of cells from the germinal epithelium occurred which gave rise to young oocytes. Grafts were made into the kidney of the male rat, the surface of the kidney being slightly injured to receive the graft.

Tamura's results demonstrated to his

satisfaction that transplantation of ovarian tissue into male mice was successful in ninety per cent of the cases (thirty-one mice, total number of experimental animals), and "in almost all these cases the germinal epithelium remained intact." ('27, p. 157). Tamura observes that these conclusions are supported by those of Schultz ('00) and of Voss ('25) in the guinea pig, contrary to the results of Marshall and Jolly ('07), who stated that in their experiments the germinal peritoneum was always absorbed. In a great number of Tamura's grafts mitotic figures were present in the germinal epithelium at about eight days after transplantation. These are similar to those observed by Allen ('23) in cyclic proliferations from the germinal epithelium at each normal oestrous period. In addition "young oocytes and successive stages of neoformation of the oocytes" were found, and Tamura believes this proliferation of cells quite comparable to those observed by Allen.

Even in the less favorable grafts where degenerative changes set in among the primary follicles, if vascularization had been established, the germinal epithelium was still active, an observation to which Tamura attached considerable importance. Young oocytes appearing before the tenth day became medium-sized follicles at about fourteen to fifteen days, and proliferation continued up to twenty days. At this point the graft attained the stage at which it was when transplantation took place, and the activity of the epithelium ceased until the second proliferation. The rhythm, however, was slower than that of the normal oestrus cycle of the female as recorded by Allen. Tamura has little doubt apparently that the source of these proliferations was the epithelium.

In working on the problem of sex-inversion in the domestic fowl, Domm ('27) was led to perform an extensive series of gonadectomies on hens. Subsequent examination revealed in a number of cases a regeneration of ovarian tissue. These Domm attributed to incomplete removal in consequence of the difficulties inherent in such an operation in the fowl. Some operations were known to be incomplete at the time of removal and regeneration was to be expected.

Domm reports some cases, however, in which regeneration followed apparently complete ovariotomy despite the fact that the ovarian region had been thoroughly cauterized. The tissue regenerated was functional to such an extent as to interfere seriously with the object of the operation. With regard to these particular cases Domm concludes that a very small fragment of ovarian tissue must have been left in place. He says: "the mass of ovarian tissue which remained behind must have been extremely small, in fact, in some cases one would wager that they were so small as to be almost invisible. Nevertheless, such fragments hypertrophy and counteract the effects of complete ovariotomy." ('27, p. 98).

An experimental study of ovarian regeneration in mice was made by Haterius ('27, '28) basing conclusions on histological study. The operative procedure was refined and precaution taken that the capsule be slit and that as little non-ovarian tissue as possible be removed. In some few cases the capsule and a part of the stalk were included in the excised tissue. To test the regenerative capacity of ovarian tissue in mice partial operations were performed. Incomplete removal was always followed by striking hypertrophy of the remaining piece, a fact also recorded by Kanel ('01), Hartman ('25), Lipschutz ('25), Slonaker ('27), and others.

Adams and Kirkwood ('28) performed gonadectomies on both males and females

of the salamander, *Triturus viridescens*, and noted, after varying periods of time, the presence or absence of gonadial tissue, the condition of the reproductive ducts, and changes in the secondary sexual characters. Of seventy-two males, examined from thirty-three days to a year after castration, sixty-four showed no testicular tissue, five showed one lobe on either right or left side, and three a lobe on each side. At the time of this first report, the evidence was being examined whether these eight cases were due to regeneration or to incomplete removal. In the sixty-four cases where no testicular tissue appeared, the Wolffian ducts and ureters were atrophied to various extents. Of nineteen ovariotomized females, examined fifty-eight to 192 days later, ovarian tissue was present in only one. All the females showed atrophied oviducts.

During the preparation of this review, an abstract describing recent experiments by Pencharz ('29a, '29b) has come to the writer's attention. Bilateral ovariotomy was performed on a total of 118 animals including both rats and mice. The age range was from twenty-five to 180 days and the period of observation seventy-five to 308 days. Complete absence of oestrous phenomena followed in all except three individuals. In these three, oestrous cycles continued, and study of serial sections of the ovarian region demonstrated incomplete removal. Contrary to the opinion of Parkes, Fielding, and Brambell ('27), Pencharz concludes that "an initial absence of cycles is not evidence of the completeness of the removal of the ovary." ('29, Wistar Institute Abstract, no. 2322, July 31). His observations led him to believe that ovarian tissue does not arise from non-germinal substance but that even a very minute fragment left intact may become extensively hypertrophied and in the natural course of events functional.

THE AUTHOR'S EXPERIMENTS ON OVARIAN REGENERATION IN THE ALBINO RAT

The immediate occasion for this review was an extensive study of regeneration in the albino rat. This work was begun in November, 1926, with a view to determining under what conditions the operator can be certain of complete removal, whether after such removal regeneration is possible, and what bearing the age of the animal has upon regeneration.

As a preliminary series, both ovaries were removed from 105 rats and each ovary was preserved for later histological study. The animals, which in this first series ranged in age from ten to two hundred days, were selected from a well-cared-for colony originally derived from Wistar Institute stock. Operative technique was simple but carefully carried out, ordinary aseptic precautions being taken to prevent possible infection. Usually both sides were operated at the same time, but occasionally, when it seemed advisable, from one to three days elapsed between the two ovariotomies. To avoid the possibility of death from anaesthesia standardized hospital ether was used, and the amount of anaesthetic administered reduced to a minimum. Small incisions were made through the skin and body wall above the ovarian region on each side of the back. Operations were performed under a powerful magnifying glass. The thin, transparent capsule of the ovary was "picked up" by means of forceps and slit with fine iridectomy scissors. The ovary was cut off at the hilus, the stalk and capsule being left in place. The tubes were injured as little as possible, and in no case were they ligated. The wounds were sutured with surgical silk and swabbed with iodine and collodion. With the exception of one or two cases recovery was rapid and uneventful.

The period allowed for regeneration ranged from ninety to 180 days. Among the 105 doubly-ovariotomized rats (210 possibilities), there were eight cases of regeneration as determined by sectioning the regenerated masses of tissue. None of the rats under forty days showed regeneration, although rats from ten to forty days of age at the time of operation were allowed the longer period in which to regenerate. The eight ovaries removed from these sites of regeneration were sectioned to determine whether the entire ovary had been removed. In two of these eight original ovaries incomplete removal was demonstrated histologically, while in six cases, extirpation was apparently complete (see Fig. 12). This gives a regeneration rate of 2.88 per cent in the rat as compared to sixty-four per cent obtained by Davenport ('25) in the mouse, five per cent by Haterius ('27), 16.6 per cent by Pallot ('28), and 3.46 per cent by Parkes, Fielding, and Brambell ('27) also in the mouse, where the ovary, capsule, and a portion of the tube were removed, fifteen per cent where only the ovary was removed.

The histology of the ovary

The adult ovary consists histologically of a frame-work of stroma and strands of connective tissue radiating out from the hilus. In this frame-work the Graafian follicles are embedded, and the whole is invested by a serous covering. Though this serous membrane or capsule is derived from the peritoneum, it differs essentially from that structure in so far as its epithelium consists of a single layer of columnar cells instead of the flattened endothelial cells of the peritoneum of other parts. This covering was termed the germinal epithelium by Waldeyer.

The frame-work or stroma of the ovary is composed of a characteristic soft tissue abundantly supplied with blood vessels. It consists for the most part of small, spindle-shaped cells, with connective tissue strands between. On the surface of the ovary this stroma is much condensed, and forms a more compact layer. This was formerly regarded as a distinct fibrous covering and was called the "tunica albuginea," a term which still is used widely. It is really nothing more than a condensed layer of the stroma.

Numerous Graafian follicles are embedded in the stroma. Immediately beneath the "tunica albuginea" the follicles in the earliest condition are found and this is termed the cortical layer or cortex. But in an ovary from the surface of which ovulation is taking place regularly, and one in which, therefore, corpora lutea appear, more mature follicles are seen side by side with younger follicles. Some atretic follicles are always present. Toward the center of the ovary the stroma becomes highly vascular, and this region is called the medullary region. It was called by Waldeyer the "zona vasculosa." This stroma forms the tissue of the hilus by which the ovary is attached (the stalk).

The histology of the regenerated bodies

The regenerated bodies in the six occurrences described here consisted of irregular masses of interstitial tissue (stroma) alternated with fibrous tissue. In some cases regenerated masses were not surrounded by a capsule as is the original ovary; and in some others the slit capsule had healed over, enclosing the regenerated tissue. Contrary to the findings of Davenport, these observations showed no apparent correlation between the presence of the capsule at autopsy and the complete removal of the original ovary. Where no regeneration took place at the site of the excised ovary the capsule was found frequently at autopsy adhering to the tube.

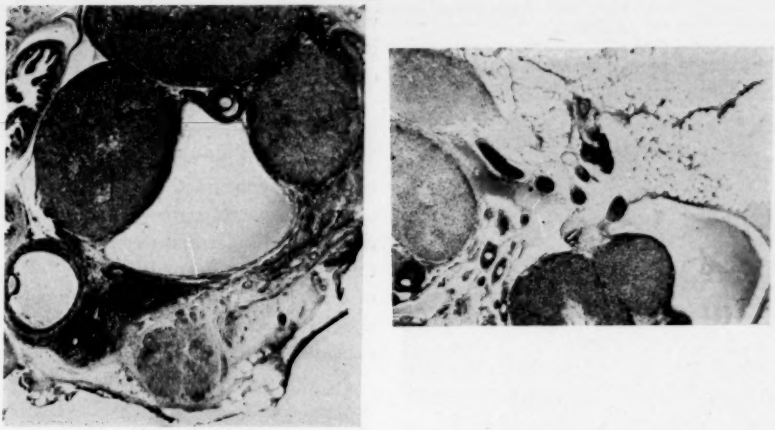

FIG. 12. PHOTOMICROGRAPHS SHOWING MICROSCOPIC APPEARANCE OF A TYPICAL REGENERATED BODY OF THE FIRST SERIES

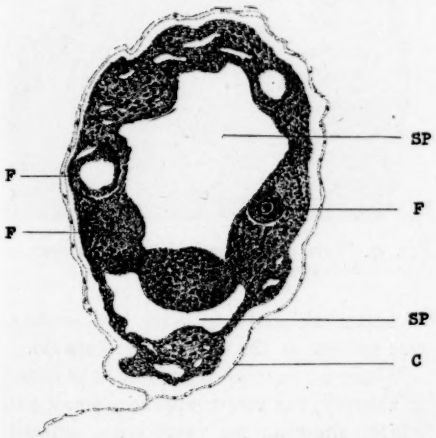

FIG. 13. SECTION THROUGH REGENERATED BODY SHOWING SPACES FILLED WITH CLEAR FLUID WHICH TAKES A SLIGHT STAIN. GERM CELLS IN THE TISSUE SURROUNDING THE SPACE

SP—space containing fluid. *C*—capsule of ovary. *F*—follicle.

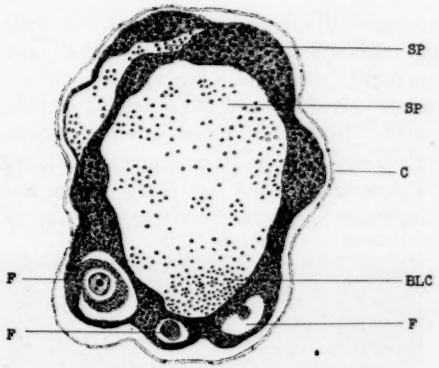

FIG. 14. SECTION THROUGH REGENERATED MASS SHOWING SPACES FILLED WITH BLOOD CELLS

F—follicle. *SP*—space filled with blood. *C*—capsule of ovary. *BLC*—blood cells.

Some sections show cut ends of the Fallopian tube, as if the body had regenerated at the terminus of the tube, and had adhered to it so that in dissecting out the regenerated body a portion of the attached tube was also excised. Frequently great hollows are seen in regenerated masses of tissue either filled with a fluid which takes a light stain and in which no cells appear, or filled with many blood cells. Cross-sections of blood vessels are numerous in the sections, and fatty tissue is always present in the regenerated masses,

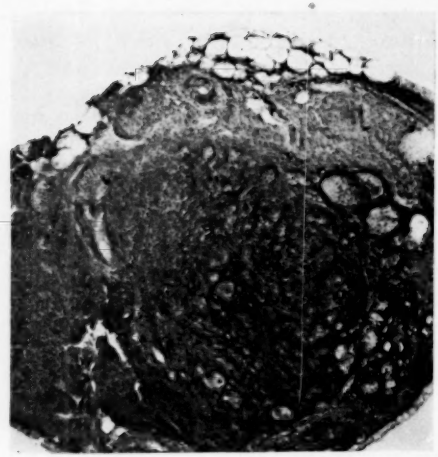

FIG. 15. PHOTOMICROGRAPH SHOWING APPEARANCE OF TYPICAL NON-GERMINAL REGENERATED MASS

occasionally in great abundance. In some of the bodies germ cells are small and scattered, while in a few the follicles are more advanced and fairly widely distributed. In the two cases in which incomplete extirpation can be demonstrated, the regenerated bodies are much larger and have an appearance nearer to that of normal ovarian tissue, indicating that where a piece large enough to be detected by sectioning the excised ovary is left at operation, the hypertrophy is striking.

Frequently a thin capsule filled with a fluid was found at the site of regeneration. These invariably collapsed when punctured, and contained either blood (haemocoele) or a clear, watery fluid (hydrocoele) similar to that found in spaces within the regenerated bodies. With the exception of one case, no germ cells were present in the tissues surrounding such a collapsed capsule. In one a small body, consisting of scattered, early follicles and stroma, was present at the edge of the capsule.

FIG. 16. PHOTOMICROGRAPH SHOWING INTERSTITIAL AND CONNECTIVE TISSUE COMPOSING NON-GERMINAL REGENERATED MASSES

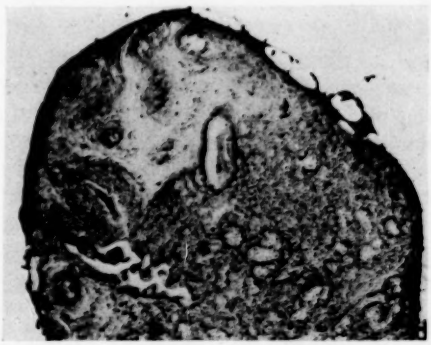

FIG. 17. PHOTOMICROGRAPH SHOWING APPEARANCE OF NON-GERMINAL REGENERATED MASS

Where no regenerated tissue was found at autopsy, the uterus appeared small and white, showing no vascularity whatsoever, the usual condition in castrated animals. Vascularity of the uterus was, however, associated with the occurrence of a hydrocoele or a haemocoele regardless of the presence or absence of a tissue-mass containing germ cells. In one instance vascularity of the uterus was prominent when the regenerated mass showed interstitial tissue but no germ cells, and when no hydrocoele or haemocoele was present, an

TABLE 1

Showing the individual operative histories of the first series. N = *negative*

FEMALE NO.	AGE AT OPERATION IN DAYS	DATE OF OPERATION	DATE OF AUTOPSY	AUTOPSY FINDINGS		REMARKS
				site right ovary	site left ovary	
Hooded 1	60	12- 9-26	5-18-27	N	N	
White 44	214	12- 9-26	5-17-27	N	Body	One horn vascular, other white. Ovaries removed very lobed.
Hooded 2	60	12-13-26	5-18-27	N	N	
White 238	46	12-13-26	5-17-27	Body	N	One horn vascular; body has large cavity in center filled with fluid. Fringe of tissue around cavity contains germ cells.
245	46	12-13-26	5-17-27	Body	N	One horn vascular; large body, much fatty tissue, scattered germ cells.
79	187	12-17-26	5-17-27	Large hydrocoele	N	No body; thin capsule filled with fluid. Uterus vascular; no ovarian tissue.
134	164	12-17-26	5-18-27	N	N	
137	164	12-17-26	5-18-27	N	Small body, hydrocoele	Body has scattered germ cells; uterus vascular.
240	50	12-17-26	5-18-27	N	N	
2458	52	12-19-26	5-18-27	N	N	
250	52	12-19-26	5-18-27	N	N	
257	52	12-19-26	5-20-27	N	Body	Body at edge of haemocoele; body composed of fat, fibrous tissue, large spaces filled with blood.
258	52	12-19-26	5-20-27	N	N	
256	53	12-20-26	5-17-27	Body	N	Large body; uterus vascular; body has well-developed germ cells and corpora lutea. Litter born 5-16 (2). Ovary at time of removal large and lobed. Incomplete removal.
277	52	12-20-26	5-20-27	Body and hydrocoele	N	Uterus vascular; body contains small, scattered follicles.
267	52	12-20-26	5-20-27	N	N	
270	52	12-20-26	5-20-27	N	N	
367	50	12-21-26	5-24-27	N	Body	Uterus very vascular. Body large, follicles and corpora lutea. Litter born 4-30 (5). Ovary lobed at removal, incomplete removal.
368	50	12-21-26	5-21-27	Hydrocoele, small body	N	Body fibrous and fatty. No germ cells. Uterus slightly vascular.
359	50	12-21-26	5-21-27	N	N	
290	62	12-21-26	5-21-27	N	N	

TABLE 1—*Continued*

FEMALE NO.	AGE AT OPERATION IN DAYS	DATE OF OPERATION	DATE OF AUTOPSY	AUTOPSY FINDINGS		REMARKS
				site right ovary	site left ovary	
White 280	62	1- 1-27	5-21-27	N	N	
288	62	1- 1-27	5-21-27	Large hydrocoele	N	Hydrocoele contained watery fluid, no follicles.
2348	62	1- 1-27	5-21-27	N	N	
Hooded 3	58	1-28-27	4-24-27	N	N	Female died 4-24, digestive disturbance.
4	58	1-28-27	5-21-27	N	Small body	Uterus vascular. Body consists of fatty tissue, no germ cells.
5	58	1-28-27	5- 9-27	N	N	Female died, 5-9, pneumonia.
6	58	1-28-27	5-20-27	Hydrocoele, small, white body	N	Uterus vascular. Body fatty tissue and fibrous tissue. No follicles.
7	48	1-28-27	5-24-27	Body	N	Uterus very vascular. Body has germ cells and corpora lutea. Two very small embryos in right horn.
8	48	1-28-27	5-24-27	N	N	
9	48	1-28-27	5-24-27	N	N	
10	48	1-28-27	5-24-27	Small body and hydrocoele	N	Uterus slightly vascular; hydrocoele filled with fluid; no follicles.
White 478	62	1-29-27	5-24-27	N	N	
477	62	1-29-27	5-24-27	N	N	
390	74	1-29-27	5-24-27	N	N	
347	91	1-29-27	5-24-27	N	N	
459	70	1-31-27	5-24-27	N	N	
456	70	1-31-27	5-24-27	N	N	
460	70	1-31-27	5-24-27	N	N	
1227	47	2- 9-27	5-24-27	N	N	
346	96	2- 9-27	5-24-27	N	N	
Hooded 12	45	2- 9-27	5-24-27	N	N	
13	45	2- 9-27	5-24-27	N	N	
14	45	2- 9-27	5-24-27	N	Hydrocoele	Uterus vascular; no body.
White 489	69	2-13-27	5-24-27	Small body	N	Uterus slightly vascular; body has no germ cells.
679	45	2-13-27	5-24-27	N	N	
990	40	2-13-27	5-24-27	N	N	
890	40	2-13-27	5-24-27	N	N	
1223	41	2-13-27	5-24-27	N	N	
1224	41	2-14-27	5-24-27	N	N	
1226	41	2-14-27	5-24-27	N	N	
590	56	2-14-27	5-24-27	N	N	
1240	36	2-15-27	5-24-27	N	N	
1238	36	2-15-27	5-24-27	N	N	
1239	37	2-16-27	5-24-27	N	N	
680	44	2-16-27	5-24-27	N	N	
1233	37	2-16-27	5-24-27	N	N	
12369	35	2-17-27	5-24-27	N	N	
1246	37	2-16-27	5-24-27	N	N	
780	44	2-16-27	5-24-27	N	N	

TABLE 1—*Concluded*

FEMALE NO.	AGE AT OPERATION IN DAYS	DATE OF OPERATION	DATE OF AUTOPSY	AUTOPSY FINDINGS		REMARKS
				site right ovary	site left ovary	
White 799	74	2-18-27	5-24-27	N	N	
889	74	2-18-27	5-24-27	N	N	
689	48	2-18-27	5-24-27	N	N	
560	54	2-20-27	5-24-27	N	N	
567	55	2-21-27	5-24-27	N	N	
568	55	2-21-27	5-24-27	N	N	
579	55	2-21-27	5-24-27	N	Small body	Uterus vascular. Body has no follicles.
1379	22	2-24-27	7-31-27	N	N	
1389	22	2-24-27	7-31-27	N	N	
1278	43	2-24-27	7-31-27	N	N	
1288	43	2-24-27	7-31-27	N	N	
1289	43	2-24-27	7-31-27	N	N	
1290	44	2-25-27	7-31-27	N	N	
1367	30	2-27-27	7-31-27	N	N	
1378	30	2-27-27	7-31-27	N	N	
1450	15	2-27-27	7-31-27	N	N	
1369	30	2-27-27	7-31-27	N	N	
1370	30	2-28-27	7-31-27	N	N	
1377	30	2-28-27	7-31-27	N	N	
1346	34	2-28-27	7-31-27	N	N	
1456	17	3- 1-27	7-31-27	N	N	
1457	17	3- 1-27	7-31-27	N	N	
1458	17	3- 1-27	7-31-27	N	N	
1459	17	3- 1-27	7-31-27	N	N	
1460	17	3- 1-27	7-31-27	N	N	
1467	17	3- 1-27	7-31-27	N	N	
1468	17	3- 1-27	7-31-27	N	N	
Hooded 15	16	3- 2-27	7-31-27	Small hydrocoele	N	Uterus slightly vascular; no body.
16	16	3- 2-27	7-31-27	N	N	
17	16	3- 2-27	7-31-27	N	N	
18	16	3- 2-27	7-31-27	N	N	
19	22	3-10-27	7-31-27	N	N	
White 1478	26	3-12-27	7-31-27	N	N	
1488	26	3-12-27	7-31-27	N	N	
1490	22	3-12-27	7-31-27	N	N	
1499	22	3-12-27	7-31-27	N	N	
1489	22	3-12-27	7-31-27	N	N	
1567	17	3-12-27	7-31-27	N	N	
1568	17	3-12-27	7-31-27	N	N	
1569	17	3-12-27	7-31-27	N	N	
1570	10	3-15-27	8- 1-27	N	N	
Hooded 24	24	3-31-27	8- 1-27	N	N	
25	24	3-31-27	7-31-27	N	N	
26	24	3-31-27	8- 1-27	N	N	
20	22	3-10-27	8- 1-27	N	N	
21	22	3-10-27	8- 1-27	N	N	
23	22	3-10-27	8- 1-27	N	N	
27	24	3-10-27	8- 1-27	N	N	

TABLE 2

Showing the individual operative histories of the second series. N = negative

FEMALE NO.	AGE AT OPERATION IN DAYS	DATE OF OPERATION	DATE OF AUTOPSY	AUTOPSY FINDINGS		REMARKS
				Site right ovary	Site left ovary	
Hooded 58	45	1-24-28	6- 4-28	N	N	
59	45	1-24-28	6- 4-28	N	N	
122	48	1-25-28	6- 4-28	N	N	
123	48	1-25-28	6- 4-28	N	N	One horn of uterus sealed by adhesion; filled with a fluid.
89	48	1-25-28	6- 4-28	N	N	
77	50	1-25-28	6- 4-28	N	N	
68	50	1-30-28	6-15-28	N	N	
69	50	1-31-28	6-15-28	N	N	
78	50	1-31-28	6-15-28	N	N	
124	49	2- 1-28	6-15-28	Body	N	Body contains no germ cells.
128	49	2- 1-28	6-15-28	N	N	
129	50	2- 2-28	6-15-28	N	N	
130	50	2- 2-28	6-15-28	N	N	
136	50	2- 4-28	6-15-28	N	N	
138	50	2- 3-28	6-15-28	N	N	
146	50	2- 3-28	6-15-28	N	N	
147	49	2- 5-28	6-15-28	N	N	
148	49	2- 5-28	6-15-28	N	N	
168	36	2- 5-28	6-15-28	N	N	
157	38	2- 5-28	6-15-28	N	N	
158	38	2- 7-28	6-15-28	N	N	
159	38	2- 7-28	6-15-28	N	N	
White 44	50	2- 9-28	6-15-28	N	N	
46	50	2-11-28	6-15-28	N	N	
47	50	2-11-28	6-15-28	N	N	
5688	24	2-14-28	6-15-28	N	N	
5680	24	2-14-28	6-15-28	N	N	
5689	25	2-15-28	6-15-28	N	N	
Hooded 177	32	3-11-28	6-15-28	N	N	
178	32	3-11-28	6-15-28	N	N	
180	32	3-11-28	6-15-28	N	N	
56	22	3-13-28	6-15-28	N	N	
60	40	3-20-28	6-15-28	N	N	
67	40	3-20-28	6-15-28	N	N	
69	40	3-20-28	6-15-28	N	N	
70	40	3-20-28	10- 1-28	N	N	
77	40	3-20-28	10- 1-28	N	N	
78	40	3-23-28	10- 1-28	N	N	
79	40	3-23-28	10- 1-28	N	N	
80	40	3-23-28	10- 1-28	N	N	
88	40	3-27-28	10- 1-28	N	N	
Hooded 190	40	3-31-28	10- 1-28	N	N	
199	40	3-31-28	10- 1-28	N	N	
223	40	4- 2-28	10- 1-28	N	N	
224	40	4- 2-28	10- 1-28	N	N	

TABLE 2.—*Continued*

FEMALE NO.	AGE AT OPERATION IN DAYS	DATE OF OPERATION	DATE OF AUTOPSY	AUTOPSY FINDINGS		REMARKS
				Site right ovary	Site left ovary	
White 89	22	4- 3-28	10- 1-28	N	N	
Hooded 225	10	4- 7-28	10- 1-28	N	N	
226	10	4- 7-28	10- 1-28	N	N	
234	10	4- 7-28	10- 3-28	N	N	
235	10	4-18-28	10- 3-28	N	N	
236	18	4-18-28	10- 3-28	N	N	
229	20	4-23-28	10-12-28	N	N	
230	20	4-23-28	10-12-28	N	N	
White 225	20	4-23-28	10- 3-28	N	N	
227	22	4-25-28	10- 3-28	N	N	
228	22	4-25-28	10- 3-28	N	N	
229	22	4-25-28	10-12-28	N	N	
230	23	4-28-28	10-12-28	N	N	
237	21	4-21-28	10-12-28	N	N	
238	21	4-29-28	10-12-28	N	N	
239	10	5- 1-28	10-12-28	N	N	
240	12	5- 3-28	10-12-28	N	N	
244	12	5- 3-28	10-12-28	N	N	
245	12	5- 3-28	10-12-28	N	N	
223	12	5- 2-28	10-13-28	N	N	
234	13	5- 3-28	10-13-28	N	N	
246	28	5- 5-28	10-13-28	N	N	
247	29	5- 6-28	10-13-28	N	N	
248	29	5- 6-28	10-13-28	N	N	
249	29	5- 6-28	10-13-28	N	N	
1249	29	5- 6-28	10-13-28	N	N	
250	30	5- 7-28	10-13-28	N	N	
256	30	5- 7-28	10-13-28	N	N	
257	32	5- 7-28	10-13-28	N	N	
258	32	5- 7-28	10-13-28	N	N	
260	32	5- 9-28	10-13-28	N	N	
267	33	5-10-28	10-13-28	N	N	
268	33	5-10-28	10-13-28	N	N	
269	33	5-10-28	10-13-28	N	N	
270	34	5-11-28	10-13-28	N	N	
277	34	5-11-28	10-13-28	N	N	
278	37	5-14-28	10-13-28	N	N	
279	37	5-14-28	10-13-28	N	N	
280	47	5-16-28	10-13-28	Body	N	Body contains no germ cells; uterus slightly vascular.
288	45	5-16-28	10-13-28	N	N	
289	48	5-16-28	10-13-28	N	Body	Body contains no germ cells; uterus slightly vascular.
290	48	5-16-28	10-13-28	N	N	
299	38	5-16-28	11- 1-28	N	N	
1299	38	5-16-28	11- 1-28	N	N	
334	38	5-16-28	11- 1-28	N	N	

TABLE 2—*Concluded*

FEMALE NO.	AGE AT OPERATION IN DAYS	DATE OF OPERATION	DATE OF AUTOPSY	AUTOPSY FINDINGS		REMARKS
				Site right ovary	Site left ovary	
White 2457	15	5-16-28	11- 1-28	N	N	
458	15	5-16-28	11- 1-28	N	N	
459	15	5-16-28	11- 1-28	N	N	
460	15	5-16-28	11- 1-28	N	N	
Hooded 260	22	5-16-28	11- 1-28	N	N	
267	22	5-16-28	11- 1-28	N	N	
268	22	5-16-28	11- 1-28	N	N	
269	23	5-17-28	11- 1-28	N	N	
270	23	5-17-28	11- 1-28	N	N	
277	23	5-17-28	11- 1-28	N	N	
278	23	5-17-28	11- 1-28	N	N	
279	23	5-17-28	11- 1-28	N	N	
280	21	5-22-28	11- 1-28	N	N	
299	21	5-22-28	11- 1-28	N	N	
347	21	5-22-28	11- 1-28	N	N	
348	21	5-22-28	11- 1-28	N	N	
245	22	5-22-28	11- 1-28	N	N	
246	22	5-22-28	11- 1-28	N	N	

observation which perhaps substantiates the conclusion of Parkes ('26, '27) that neither the Graafian follicle nor the corpus luteum is necessary for the maintenance of uterine tone. The correlation between the occurrence of a capsule filled with a fluid or with blood and the vascularity of the uterus suggests the presence of a hormone (perhaps from interstitial tissue) which maintains the condition of the genital organs.

Preliminary reports of the first series were made in 1927 (also 1927b published 1929) and a general statement of the results of both series in 1929. Table 1 gives the operative history of the animals of the first series.

The influence of age on regeneration

The fact that no rats of the first series under forty days of age showed regeneration suggested that there *is* a correlation between the possibility of regeneration and the age of the animal at the time of operation, and that the younger the animal when spayed, the less likelihood of regeneration. From a study of the first series it seemed that the chance of success in complete removal of the ovary increased as the age of the animal decreased.

With these facts in mind a second series, comprising rats under forty days of age (range ten to forty days) was initiated. One-hundred-eight rats were operated. Both ovaries were removed. The operative technique was identical with that employed in the first series. As a check on those under forty days of age, a few operations were performed on rats over forty days of age. Twenty-three of the 108 ranged in age from forty to fifty days. In all except three of this series the autopsy findings were entirely negative, the uterus in each case being very small and anemic. No trace of regenerated tissue was present. In each of three operated animals (age forty-seven to fifty days) a small body was present at the site of one excised ovary, the other site being negative. It is interesting to note that these

three were among the older rats operated as a check on the younger ones, so that in this series, as well as the first, no rats under forty days of age showed regeneration. Table 2 gives the operative history of the rats of the second series. In the three showing regenerated tissue the uterus at autopsy was vascular. The three regenerated masses, which were studied histologically and carefully examined for follicles, consist of small amounts of interstitial tissue, fibrous tissue, and fat, and show no cells resembling germ cells. The second series of operations is thus one hundred per cent negative.

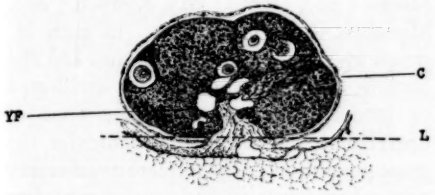

FIG. 18. SECTION THROUGH OVARY OF YOUNG RAT SHOWING SMALL, COMPACT OVARY

YF—young follicles. *C*—ovarian capsule. *L*—line of excision.

It seems to follow from these observations that the success of complete extirpation depends primarily on the age of the animal at the time of operation. The immature ovary of young rats is a small, ovoid body, freely movable, and not yet embedded in fat. When the thin capsule is slit by means of sharp scissors, the small, compact ovary "pops out" of the capsule. It can be cut off at the hilus easily and quickly. There is no bleeding from small capillaries to obscure the picture, since the characteristic vascularity of the region has not yet developed. In older rats, occasionally just beyond fifty days, and especially after maturity (about sixty-five days) the ovary is surrounded by fat and is very irregular in shape, owing to the presence of numerous follicles and corpora lutea at or near the surface. In a number of instances a large lobe of the ovary was buried under the anterior end of the coiled tube. Such a lobe is easily overlooked at operation. Some bleeding from small vessels is always to be expected in the adult rat, notwithstanding all precautions to prevent it. This obscures the region somewhat, and makes complete removal of the lobed body difficult. In the two cases in the first series in which incomplete removal was demonstrated by

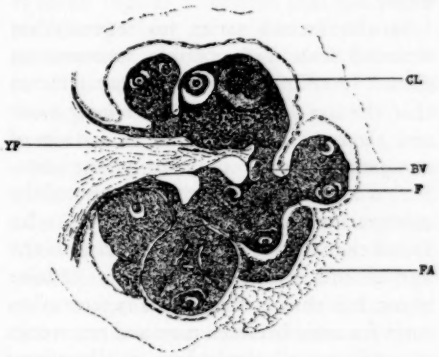

FIG. 19. SECTION THROUGH THE OVARY OF MATURE RAT, SHOWING THE LOBED CONDITION

Dotted lines indicate points at which a lobe might be cut off and left in place at excision. Sectioning in these planes might not reveal the absence of the lobe from the excised ovary. *YF*—young follicles. *F*—follicle. *FA*—fatty tissue.

sectioning the excised ovary, this was apparently the explanation. In both cases hypertrophy of the remaining piece followed, and young were subsequently born to both females.

From a study of variation in the shape of the mature ovary it seems that in some cases a lobe of the ovary may be almost constricted off from the rest. Several such cases came to light during the course of these experiments. In some instances this constriction was deep enough so that if the ovary were cut at this point, it could not be detected by sectioning the excised

piece. Thus a considerable amount of ovarian tissue might remain behind at operation, and, if the ovary were sectioned in the plane of the constriction, a study of the sectioned ovary might not reveal its absence. Large adult ovaries were sectioned in different planes to test such a possibility. There is evidence that this is the explanation in the cases of the first series where the excised ovary appeared complete, and yet regeneration occurred. In young rats such a difficulty is eliminated.

In the second series no regeneration occurred from 216 possible regeneration sites. It seems from these experiments that the *age factor* is the *determining factor* and that the operator can be certain of complete removal only in young rats. Such a conclusion is just the reverse of the observations of Davenport ('25), who found that throughout the experiment the age of the animal had no very definite effect, but that in some cases regeneration rates for mice between nine and ten weeks of age were relatively low, while others at four weeks gave as high as eighty-three per cent.

Regeneration probably due to incomplete removal of ovary

When complete removal is possible, as in young animals, no regeneration follows, and it seems plausible to believe that the regeneration in older animals which occurred in these experiments, and perhaps those of other workers, was due wholly to the difficulties attendant upon a perfect ovariotomy.

It is a well-known fact of breeder's experience that castration in the male of fowls, horses, cattle, swine, etc., is not followed by regeneration of the testis. In the male the gonad is a discrete, freely movable body, and complete removal is not difficult as it is with the lobed ovary of the female. The history of the human race supplies similar evidence. Castration was practised extensively in antiquity and still is practised in some oriental countries. So far as is known no cases in which normal male characteristics returned after early castration have ever been recorded.

Numerous instances are recorded in medical literature in which normal cyclic function was re-established and pregnancy subsequently occurred in women after removal of both ovaries. Clinical cases of this kind have been reported by Robertson ('90), Gordon ('96), Sutton ('96), Morris ('01), Doran ('02), Kynoch ('02), Meredith ('04) and others. In each instance the return of menstruation and the occurrence of pregnancy were attributed to incomplete removal at the time of operation. Meredith ('04) indicates the great possibility of incomplete ovariotomy even when care is taken to secure complete extirpation. He says (p. 1361):

> In my own cases, the re-establishment of menstruation followed by pregnancy, is, of course, to be explained only by the theory that some portion of ovarian tissue capable of maturing follicles was left untouched by the operation, and further that the potency of one or other Fallopian tube was subsequently restored. The possibility of this occurrence has been fully established and need not, therefore, be discussed. On the other hand, the question of the probable site of the oöphoritic tissue which escaped removal requires some brief consideration.

He refers to the possible existence of a third ovary, the occurrence of which had been previously described by some German gynecologists, but considers such an occurrence highly improbable. He explains his own cases as a question of an outlying portion of ovarian tissue in connection with the uterine extremity of one of the ovarian ligaments. Such a condition has been observed clinically and recorded in the literature.

SUMMARY

A general survey of the literature reveals four groups into which contributions dealing with the origin and history of definitive germ cells may be divided.

I. Those who deny early segregation of germ cells and believe that germ-cell formation is a matter of the differentiation of somatic cells.

II. Those who admit early segregation of germ cells, but conclude that such cells are not definitive and degenerate, to be replaced by proliferations of new cells from the epithelium.

III. Those whose investigations have led to the conclusion that germ cells are segregated early and migrate to the site of the developing gonad to persist as definitive ova or sperm, but that their numbers are increased periodically by proliferations from the epithelium.

IV. Those who believe that the definitive germ cells are set aside at an early stage in embryonic development, not to be replaced later by transformations of differentiated peritoneal cells. Their numbers are increased only by mitotic divisions.

The approach made from the standpoint of the regeneration of the gonad following removal throws light upon the problem of the definitive germ cells. If after extirpation of all gonadial tissue, the gonad is even partially replaced by peritoneal proliferation, certainly this is evidence of the transformation of soma cells into germ cells. And if under optimum conditions gonadial tissue does not reappear, it is safe to conclude that soma cells do not proliferate germ cells.

The writer's experiments seem to show that it is easily possible to be certain of complete removal of the ovary in young rats (under forty days); and that upon complete removal no regeneration occurs. It seems logical to believe that the regeneration in older animals in these experiments was due to the difficulties inherent in a perfect ovariotomy. Thus the age factor becomes the determining factor. In operations performed on very young rats, when the capsule as well as the stalk remained in place, ample opportunity was afforded for proliferation from the epithelium, if somatic tissue has the power to proliferate generative cells. If no regeneration occurs under these conditions, it follows that the epithelium cannot regenerate the excised ovarian tissue. Thus in so far as these experiments bear on the problem of the definitive germ cells, they lend no support to origin from a peritoneal source. There is still some evidence that Weismannian continuity may be a tenable hypothesis.

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THE RÔLE OF BACTERIA IN THE NUTRITION OF PROTOZOA

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INTRODUCTION

ACCORDING to Calkins (1) four principal types of nutrition are to be found among the protozoa. Some are holozoic or holophytic, dependent for maintenance upon other living organisms as sources of food. Others have developed a saprozoic or saprophytic mode of nutrition and are able to live on dead organisms or the products of their disintegration. A third group is autotrophic. The presence of a photosynthetic pigment permits the organism to utilize the energy of sunlight in the elaboration of complex tissue constituents from the simplest of raw materials. Finally there are heterotrophic protozoa which are able, as has been fairly well demonstrated, to live both saprophytic and autotrophic modes of existence. Many colored flagellates are autotrophic in light and saprophytic in the dark. In fact the saprophytic flagellates are conceivably derived from heterotrophs by loss of the photosynthetic pigment.

In this paper we propose to confine our attention to nutrition of the first two types and, in particular, we shall enquire into that knotty problem of forcing a normally holozoic animal to lead a saprophytic existence. Our purpose in so doing is not only to attempt the teaching of new tricks to the protozoa. Nor do we care merely to assist in unravelling the threads of inter-related fact that are so confusingly tangled in the baffling problems of holozoic nutrition, even though a satisfying explanation of these phenomena would constitute one of the most fundamental contributions to our knowledge of nutrition. Rather, we have found ourselves lured on by an objective of different and perhaps more immediate consequence. It is our intention to study the chemistry of protozoan metabolism, the nature and significance of those elementary and molecular constituents of protoplasm, which though present in very small quantities are nevertheless indispensable for the maintenance and well-being of the organism, the nature and mode of action of toxic agents, the effects of radiation of high intensity, in short a number of problems which demand that the protozoon under investigation be unaccompanied by other living forms. If a normally holozoic organism is to be studied along these lines it is apparent that the creature must, if possible, be led into the ways of its saprophytic cousins.

Specificity in selection of food

One of the first considerations of great importance is the surprising measure of specificity that normally prevails among

the holozoic feeders. Thus we are reminded that the holotrich *Actinobolus radians* prefers to dine only on *Halteria*, while the active ciliate *Didinium nasutum* concentrates its predatory attacks on Paramoecium. Incidentally their exploits in food-getting are full of thrills. In the words of Calkins (2) "next to the capture of *Halteria grandinella* by *Actinobolus radians* I know of nothing more spectacular or amazing in the whole realm of microscopy than the seizure and ingestion of Paramoecium by Didinium." The Suctoria seem to relish certain of the ciliates, other protozoa ingest principally a given flagellate, and so the specialization continues. [The co-existence of paramoecia and unicellular algae appears to be true symbiosis, rather than a selective digestion of algae as food by Paramoecium (3, 4).] Indeed the work of Lund (5), Mast, Schaeffer, and others indicates that discrimination in the selection of food is general among the infusoria.

Among the bacteria-eaters the same selectivity is to be found. In 1897 Frosch (6), who succeeded in culturing *Amoeba nitrophila*, a soil form, on pure lines of bacteria, observed that several were totally unsatisfactory as food for the amoeba, others were fair, and one proved to be excellent. For twenty years, the admirable pioneer work of Frosch, Tsujitani (7), Beijerinck (8) and Mouton (9) in this difficult field was almost completely overlooked or ignored. The exhaustive work of Musgrave and Clegg (10) is an outstanding exception. Though it was realized quite well that the bacterial flora of the infusions used in culturing protozoa was the most important variable, few serious attempts were made to control it. In the words of Hargitt and Fray (11) (describing the cultivation of Paramoecium in hay infusions), "it is rather striking that not a single effort has been made by modern methods to analyze the hay infusion bacteriologically." In 1917, however, Hargitt and Fray (11) plated out the bacteria from normal and abnormal hay infusions. Examination of the dominant strains showed that eight or more used singly as food for bacterial-free Paramoecium (*aurelia* and *caudatum*) were quite unsatisfactory. The division rate relative to that obtaining in a mixed bacterial flora was markedly depressed. Extinction of the protozoon line followed within twelve days. Only one strain seemed promising. On *B. subtilis* the division rate over a fifteen day period was 1.31 compared with 1.14 in the reference mixed culture. However, the *B. subtilis* experiments were few in number and of short duration. "It seems clear" concluded Hargitt and Fray "that cultures of mixed bacteria are, as a rule, far superior as a diet for Paramoecium to any one kind of bacteria. . . . . It should be possible" they add "by using cultures of bacteria, mixing these known forms in various combinations in sterile infusions and growing Paramoecium therein to secure a mixture which would be better than the ordinary mixed cultures . . . . ." Calkins (12) seems to have held the opinion that *B. subtilis* was probably the principal food of Paramoecium in hay infusions. The work of Musgrave and Clegg (10) demonstrated striking selectivity in the utilization of bacteria as food by the amoebae. Undoubtedly the most extensive inquiry into the discriminations that prevail among the protozoa in the choice of food has been pursued by Oehler of Frankfurt (13–17). A series of papers published between 1916 and 1924 reveal some surprising differences in holozoic nutrition among the protozoa. "Wenn man in dieser Weise, Amöben auf eine Bakterienreinkultur zu überführen sucht, so zeigen sich

merkliche Unterschiede. Bei manchen Bakterien gelingt die Überführung leicht, bei anderen schwer oder gar nicht." (13). Among the amoebae it was found that *Hartmanella aquarum* and *Vahlkampfia magna* would assimilate any of the bacteria tried except the timothy bacillus. *B. bulgaricum* and a certain soil staphylococcus were also not acceptable. But yeast (*Saccharomyces exiguus*) and several small amoebae were ingested. In addition it was observed that all five amoebae preferred gram-negative bacteria to gram-positive forms. Bacteria from young cultures were found better than those from old. Some rather resistant strains proved to be edible if eaten young. Bacterial spores, mold mycelia and spores, unicellular algae, and diatoms were refused by all five amoebae. Flagellates and ciliates, so Oehler reported (14), would live equally well on gram-negative and gram-positive bacteria. The timothy bacillus, though refused by amoebae, was accepted by the flagellates and ciliates. The former would eat all bacteria examined but not the yeast, *Saccharomyces exiguus*, which was probably too large. The ciliate *Colpoda Steini* would digest both yeast and mold spores. Phillips (18) reported the interesting observation that *Paramoecium aurelia*, which grew fairly well on her C′ strain of bacteria with a division rate of 1.03 over a seven month period, showed an enhanced rate of reproduction of 1.79 on the mixture A′ and C′; this despite the fact that A′ alone was incapable of supporting the growth of Paramoecium. C′ was a streptothrix. Nine other pure lines of bacteria were examined but, singly or in the twelve combinations tried, they failed to suffice. Cutler and Crump (19) have also investigated the nutritive value of different strains of bacteria in the maintenance of Hartmanella. They were able to show that the poor nutritive quality of two species of bacteria used by them was not due to the formation of toxic products. In some instances it is doubtless true that the failure of a protozoon to feed on a given bacterium is due to the formation of carbon dioxide, ammonia, trimethylamine, or other noxious substance as a product of bacterial metabolism (13). It is of interest in this connection that the diphtheria toxin liberated in a culture of diphtheria bacillus is apparently innocuous to three ciliates studied by Oehler (16). The inadequacy of a given bacterial species for protozoon nutrition may in some instances be due to the establishment of an unfavorable hydrogen ion concentration in the medium in consequence of bacterial growth. In other cases the size or shape of the bacteria may be unfavorable. It is also possible that the protozoon requires certain accessory food factors which are not to be found in all bacteria. Finally it is conceivable that the protozoon is unable to elaborate its protoplasmic constituents from the fairly simple substances utilized by the higher animals. The assimilation, without preliminary hydrolysis and subsequent formation, of highly organized substances may be necessary in this group. If so there is the possibility that these complex nutrients are of limited occurrence among the bacteria. Certainly, the presence of proteolytic enzymes in protozoon extracts (9) cannot be considered proof that proteolysis precedes the utilization of ingested protein. Most recently, Cleveland and Sanders (20) have reported definite selectivity in the utilization of bacteria by *Entamoeba histolytica*.

The technique of sterilizing protozoa

A second consideration of great importance is that of rendering protozoa bacterial-free, for only after securing a

sterile strain can one investigate the conditions of saprophytic growth on synthetic media. Four principal methods have been employed, sterilization of cysts, washing, negative geotaxis, and cataphoresis. The last of these was introduced by Amster (21), who succeeded in freeing ciliates of bacteria by inserting non-polarizable electrodes in the suspension of organisms. 0.05 per cent sodium chloride was added for conductivity. The ciliates moved to the cathode and the bacteria to the anode. Six repetitions were sufficient to sterilize the protozoa. It seems improbable that this method of sterilization would be of general utility and applicable to all bacteria. The electrical charge possessed by bacteria varies with species and hydrogen ion concentration (22) (23). Amster studied the ciliate Balantiophorus which he cultivated, uncontaminated with foreign bacteria, on a single but unidentified species in 0.1 per cent Witte peptone. The method of negative geotaxis seems to have had a limited trial among a few workers. It takes advantage of the fact that some protozoa when confined in a tube of media cluster about the surface. The accompanying bacteria, meanwhile, disperse themselves throughout the fluid. It is assumed therefore that after many serial transfers of the surface portions to fresh tubes of sterile media, the bacteria will be diluted out. This method has never received a satisfactory critical study. Washing of the protozoa in sterile water seems to have been employed the most. Hargitt and Fray (11) washed the protozoa free of bacteria by running them one at a time through five portions of sterile wash fluid in covered depression slides. The transfers were made with sterile micro pipettes. The final wash fluid and the fully bathed animals are said to have been sterile. Peters (24) used essentially the same procedure but limited his sterility tests to the final wash fluid. Phillips (18) modified the procedure slightly but seldom tested the washed protozoa for sterility. This omission served as the basis of Parpart's criticism (25) and led to the recommendation of another simple but important modification. Parpart found that five washings, 8 animals at a time, gave a sterile final wash fluid but even after 10 washings in 6 out of 8 trials the animals themselves were infected. Acting on the assumption that Paramoecium had ingested bacterial spores which therefore escaped removal by the washing process, Parpart halted the procedure while the animals were in the fifth wash fluid for 5 hours. This provided time for the defecation of spores. Four final washings then followed. The resultant animals were sterile. Still another method, one which found particular favor among the earlier workers, was that of Frosch (6). It consisted in sterilization of the protozoan cysts. Frosch sterilized old cysts of *Amoeba nitrophila* by immersion in saturated sodium carbonate at room temperature for 3 days. Young cysts were not sufficiently resistant for this drastic treatment. Non-sporulating bacteria were killed. Concentrated sodium chloride and sucrose were also of value. More recently, Severtzoff (26) has reported success in sterilizing amoeba cysts with toluene, chlorine, and calcium sulphide. Tsujitani (7) resorted to desiccation of the cysts, while Walker (27) observed that moist heat at 70°–75° for 1 hour was sufficient to kill non-sporulating organisms without injury to amoeba cysts. Oehler (17) found that long heating of the cysts (six weeks at 37° or several hours at 60°–64°) was successful. These observations are in need of confirmation. Oehler contended

that it is almost impossible to free ciliates of bacteria by washing.

If merely a mono-bacterial strain of a protozoon is desired, two methods have been reported satisfactory. The first, that of Beijerinck (8), is the oldest in protozoology. It has been of particular service in studies upon amoebae, though other protozoa may be employed. It consists in streaking agar plates radially or by a central circular smear with the strain of bacteria upon which the protozoon is to be nourished. The center of the plate is then inoculated with amoebae from the stock mixed culture. The amoebae feed upon the new bacteria and travel towards the periphery leaving the old contaminants behind them. By this means Beijerinck developed pure lines of *Amoeba nitrophila* and *Amoeba zymophila* on acetic acid bacteria, *Saccharomyces apiculatus*, and *B. coli communis*. Tsujitani (7) grew three kinds of amoebae in mono-bacterial culture on cholera bacilli, typhus bacilli, *B. coli communis*, *B. fluorescens*, *Staphylococcus pyogenes aureus*, *B. pyocyaneus*, *B. ruber*, and three or four other forms. Mouton (9) secured a fine culture of an amoeba on *B. coli communis*. Other bacteria were less satisfactory and *B. anthracis* was poor. A second procedure developed by Oehler (14, 17) consisted in replacing one bacterial strain by another through change of medium. Thus *Colpidium colpoda*, contaminated with several species of bacteria, was added to a pure culture of hay bacillus in 1 to 2 per cent peptone. The other bacilli associated with Colpidium were suppressed, leaving the hay bacillus. The addition of sterile urine and inoculation with *B. prodigiosus* caused the suppression of all bacteria but the latter, so Oehler reports. There resulted a pure line of Colpidium on *B. prodigiosus*. Likewise the use of a sugar-peptone medium permitted replacement by *B. coli communis*. Complete sterilization of Colpidium was never accomplished by Oehler. In our own experiments with the hypotrich *Euplotes taylori* we found that success in sterilization by washing was largely dependent on the quantity of bacteria. The time spent in the various baths is also an important factor.

Attempts to rear protozoa saprophytically

Of great significance are the attempts which have been made to rear protozoa saprophytically. Tsujitani (7) appears to have been the first to study saprophytic nutrition in the protozoa, although it should be mentioned that Kartulis (28) some years before reported that liver abscesses containing the dysenteric amoeba had been found by him to be free of bacteria. Cleveland and Sanders (20) have recently succeeded in producing bacteria-free amoebic abscesses in the livers of cats. In vitro, they were unable to cultivate the amoeba (*E. histolytica*) in the absence of living bacteria. From a hay infusion Tsujitani isolated a non-sporulating bacterium, which though heated to 60°–70° for 40 minutes would still serve as food for amoebae. Frosch (6), on the contrary, was unsuccessful in growing his amoeba on dead bacteria or on digests or extracts of bacteria. Musgrave and Clegg (10), likewise, were of the opinion that other living organisms were indispensable for the nourishment of amoebae. Frosch concluded that the amoeba was not a saprophyte "sondern ein Lebewesen, das zu seiner Ernährung bestimmter lebender Elemente benötigt, die anscheinend nur im lebenden Organismus vorhanden sind." The same opinion was expressed by Casagrandi and Barbagallo (29): "Man kann wohl sagen, dass es unmöglich ist, eine Amöbenkultur zu haben, ohne dass man zu gleicher Zeit sich Bakterien darin entwickeln sieht."

Tsujitani's observations remained unconfirmed for nearly 20 years. In 1911, Wülker (30) in his excellent review on amoeba culture, felt constrained to point out that "eine genaue Nachprüfung dieser bis jetzt unbestätigten Versuche ist sehr erwünscht." In 1916, Oehler reported the first of his observations which served to confirm and greatly extend the work of Tsujitani. Oehler found (13) that sterile Hartmanella and Vahlkampfia would eat and digest all bacteria, killed at 100°, which were examined. Three other sterile strains of amoebae could not be so maintained. Of the latter, however, one would ingest bacteria killed by heating at 56° for 1½ hours. The second could be maintained on *B. fluorescens* if killed at 45° for 1½ hours, but the third refused all "cooked" food. Heat-killed coli, cholera vibrios, proteus, fluorescens, sarcina, and yeast were used in these experiments. Among the ciliates, Oehler found (14) that the small forms seemed most adaptable to a diet of dead bacteria. *Colpoda Steini*, sterilized after great difficulty, would live and multiply on *B. coli* heated to 100° for 1 hour or 56° for 1½ hours. Heated yeast and heat sterilized suspensions of finely powdered casein, edestin, and muscle powder were also adequate for nutrition of *Colpoda Steini* and the flagellate Prowazekia. Heated blood serum (64°–74°) was found to be a good sterile food for sterile amoebae (17). Curiously enough, boiled spinach was excellent. Bacteria killed with ether or acetone were seldom satisfactory. Fat droplets, red blood cells, fibrin, starch grains, milk, and egg yolk were never adequate (13). All experiments with soluble foodstuffs were unsuccessful (31). Peters (24), on the contrary, reported excellent results in the cultivation of sterile *Colpidium colpoda* on a very simple synthetic medium of soluble constituents. The organic compounds employed in the first medium were merely three amino acids, glucose, and ammonium lactate. In other experiments ammonium glycerophosphate was found to be sufficient. The ciliate multiplied to over 10,000/cc. The organisms were sterilized by washing. Several, being unsuccessful in similar attempts, have insisted that Peters' sterility tests were not sufficient. It is contended that bacteria were present upon which Colpidium fed. Incidentally, Oehler never succeeded in maintaining *Colpidium colpoda* on anything but live bacteria (15). (Since this paper was submitted for publication, others in this University and ourselves have succeeded in cultivating *Colpidium colpoda* in bacteria-free media.)

Quantity of food

Several miscellaneous factors, of importance in the nutrition of protozoa, remain to be disposed of before passing on to the experimental portion. One of these, carefully investigated by Cutler and Crump, is that of the quantity and quality of food. We have already considered the latter at some length except for one phase to which Cutler and Crump in particular made a valuable contribution (32). They devoted themselves to a study of the effect of age on the reproductive rate. Working with *Colpidium colpoda* and *Oicomonas termo* they found that the division rate of organisms from a 24 hour parent cell community was much higher than that of organisms taken from a culture 4 or 5 days old. They used a simple synthetic basal medium. Oicomonas was fed on 3 or more strains of bacteria contained therein. Colpidium was associated with a stout bacillus and in addition was fed with *Sarcina lutea*. Accordingly there was not a rigorous control of the bacterial flora. Likewise Robertson (33) observed

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that a single Enchelys from a culture one day old multiplied to 38.4 in 24 hours. If the parent community was 2 days old, the multiplication was reduced to 5.9, if 3 days old, 2.6, and 4 days old, 2.0. In many instances the lowered fission rate is due to toxic metabolic products carried over from the old cell community. It is possible too that organisms from old cell communities are depleted of some essential growth principle. Thus Beers (34) has shown that starved paramoecia fed to Didinium result in the degeneration of the line as evidenced by decreased fission rate, increased death rate, and production of abnormal individuals. On the contrary the control line on well-fed paramoecia continued in a vigorous, flourishing state. Cutler and Crump also showed (19, 35) that the rate of division of protozoa is a function of the quantity of food. Thus a contaminated line of Colpidium fed with increasing proportions of *Sarcina lutea* showed the following striking changes in the division rate for 24 hour periods.

NUMBER OF BACTERIA PER COLPIDIUM	DIVISION RATE (AVERAGE)	NUMBER OF BACTERIA PER COLPIDIUM	DIVISION RATE (AVERAGE)
250	0.1	16000	0.7
500	0.1	32000	1.5
1000	0.3	64000	2.4
2000	0.3	128000	2.9
4000	0.3	256000	3.9
8000	0.4	512000	4.1
		1024000	5.3

Incidentally, removal or reduction in numbers of the contaminating bacillus from Colpidium caused degenerative changes.

Allelocatalysis

Reference has already been made to the possible existence of a growth-promoting principle in protozoa. This hypothesis was first advanced by Robertson (33), who showed in the case of Enchelys that the initial lag phase was followed by a period in which there seemed to be a mutual acceleration of growth on the part of the protozoa. In any case the division rate of an organism contained in a small volume of medium was demonstrably greater than that of an organism contained in a large volume. Both organisms used in the inoculation were of course drawn from the same parent community. Robertson postulated the existence of a growth-promoting principle described as substance X which was considered to be of nuclear origin. It was liberated into the surrounding medium on cell division. With this assumption it follows at once that the concentration of X would be greater if the initial volume of medium be small than if it be large. As a corollary it is apparent that one important rôle of bacteria could be that of serving as a source of a similar X principle, in addition to the recognized function of serving as food. Robertson bolstered up his hypothesis and elevated it to the plane of sound theory by showing that growth-promoting principles could be extracted in crude form from yeast. He did not discuss the possibility, neither did Cutler and Crump (36), nor Gregory (37), that extracts of yeast, bacteria, protozoa, and bios preparations may exert their growth-promoting effect by serving as organic foodstuffs for the enrichment of the associated bacterial flora. The observation reported by Peters (24) that an isolated protozoon would not grow in 1 cc. of medium although 20 to 40 organisms would do so, has been confirmed by many. It obviously lends support to Robertson's theory of allelocatalysis. Likewise Yocom's observations (38) on Oxytricha fit in well with this hypothesis. Arrayed against it, however, are the findings of

Cutler and Crump (36) on *Colpidium colpoda*, Myers (39) on *Paramoecium caudatum*, of Greenleaf (40), Woodruff (41), and probably many others whose findings we have not recorded. There is great need for the re-investigation of this important problem under rigid bacteriological control.

EXPERIMENTAL

The Organism

The protozoon used in our investigations was the hypotrich, *Euplotes taylori*, first described by Garnjobst in 1926 (42). The organism is a marine form common in tide pools and brackish waters in the San Francisco bay region. It is of special interest because encystment, to which it is subject, may be induced experimentally. Excystment is also amenable to control. Salt concentration is one of the significant determining factors. This important phenomenon is now receiving extensive investigation.

In addition the organism is to be employed in a study of the effect of X-rays of great intensity, in the course of which the whole animal or parts thereof will be irradiated. Morphological and chemical changes resulting from this treatment will be investigated.

For the purposes of this investigation we have devoted ourselves for some months to experiments on the nutrition of *Euplotes taylori* with the object before us of cultivating the organism in a simple synthetic medium. In this paper we shall demonstrate that the basal medium may be of great simplicity and the bacterial flora amenable to rigid control. We have not yet achieved success in culturing the organism saprophytically although we do not consider the maintenance of the ciliate in a bacterial-free medium to be an unattainable goal.

Sterilization of Euplotes taylori

A satisfying inquiry into the nutrition of the protozoon presupposes that it may, for experimental purposes, be rendered free of bacteria. The method which we have ultimately found to be adequate is, in principle, that of Hargitt and Fray (11). The process consists in the transfer of 10 to 15 Euplotes through 10 to 15 sterile baths in series. As containers of the washing medium, we have employed small watch glasses, arranged in individual Petri dishes. The transfers are made with capillary pipettes drawn from #6 glass tubing to a length of about 10 cm. and to a distal diameter of about 0.3 mm. The opposite end of the pipette is plugged with cotton and inserted into a piece of rubber tubing about 30 cm. long. The application to this tube of suction by mouth permits a delicacy of control in operation of the pipette that we have been unable to duplicate with the usual rubber bulbs. A new pipette is used for each transfer. After use it is discarded permanently. During the transfer the cover of the Petri dish is raised just enough to permit insertion of the capillary portion of the pipette. A binocular dissecting microscope is essential.

All glassware is sterilized by heating to 170° for 2 hours. Aseptic precautions are necessarily employed throughout.

The washing medium, of which 2 cc. are placed in each watch glass, consists of sterile 1:1 artificial sea water. This is prepared according to the following formula which is based, in turn, upon the sea water analyses of Page (43) (Cf. also Harvey (44)).

	grams
Sodium chloride	26.10
Magnesium chloride ($MgCl_2 \cdot 6H_2O$)	6.20
Magnesium sulphate ($MgSO_4 \cdot 7H_2O$)	4.07
Calcium sulphate, anhydrous	1.15
Potassium chloride	0.60

Disodium hydrogen phosphate.....	0.01
Ferric chloride ($FeCl_3$).....	0.01

The salts are dissolved in twice distilled water and the solution diluted to a volume of one liter. The artificial sea water thus obtained is diluted with an equal volume of distilled water and designated 1:1 ASW. It is sterilized shortly before use by filtration through a sterile Chamberland candle. The salt content of 1:1 ASW was found by experiment to be the optimum for the culturing of *Euplotes taylori*.

From 0.01 to 0.05 cc. of the fluid of each bath is carried over in the transfer of organisms to the next bath. Successful washing requires as long as 8 hours, the Euplotes being allowed to swim about in each bath for from 20 to 30 minutes (one to two hours in the middle bath), to rid themselves of bacteria. (We now permit the organisms to remain in the middle bath overnight.) After they are transferred from their last bath to the medium in which they are to be grown, 0.1 cc. samples of this medium and of the last bath are placed upon nutrient agar slants, as tests of sterility. More recently pour plates of the entire last bath have been made. A more detailed study of the washing is now in progress.

In order to determine whether these ciliates, sterile as far as their exteriors are concerned, later defecate bacteria or bacterial spores, which thereby contaminate the medium, the following experiment was tried: Euplotes, washed through 9 to 10 baths, were placed in 2 cc. of sterile bran extract in 1:1 ASW and 0.1 cc. portions of this medium transferred to agar slants on each of the 5 following days. This experiment was repeated 5 times. No contaminated slants resulted. The protozoa themselves were not tested for sterility.

Culturing Technique

Watch glasses in Petri dishes are used not only for washing of the organisms but also for their cultivation. Direct microscopic examination of the culture is thus possible without opening of the vessel. The form of the dish also permits maximum exposure of the organisms to air. From several preliminary experiments in other vessels, particularly in tubes, we are convinced that *Euplotes taylori* grows better in watch glasses than in apparatus where the medium has but a small air surface.

The culture medium, sterilized by filtration, is pipetted in $\frac{3}{4}$ cc. portions into the sterile culture vessel. The washed organisms are added, a sterility test is made, and the dish closed with a strip of surgical adhesive tape. This helps to prevent contamination and minimizes evaporation.

Growth of Euplotes taylori on isolated pure strains of bacteria

One of the first media employed by us in preliminary work was an extract of wheat bran in 1:1 ASW. The bran extract was prepared by boiling 1 gram of wheat bran for 5 minutes in 100 cc. of twice distilled water. Five cubic centimeter portions of the extract were then added to 95 cc. portions of 1:1 ASW. Mass cultures of *Euplotes taylori* were obtained for introductory experiments by adding to the medium contained in Syracuse glasses, 100 or so unwashed Euplotes and permitting the entrance of atmospheric bacteria by exposure to the air. In a few days a well populated culture was usually obtained.

In order to determine some of the bacterial strains which served for the nutrition of the protozoon, these thriving bran extract cultures were plated out.

Five dominant varieties were isolated. One was recognized as *Sarcina citrea*, a second gave pink colonies and was possibly *Rhodococcus roseus*, while the remaining three which escaped identification are designated here as A, B, C. The classification of the saprophytes is very incomplete and we have had to content ourselves thus far with determining their reactions in the usual standard media.

When washed Euplotes were added to the sterile bran extract medium inoculated with one of these five strains of bacteria, it was found that the first two tested in the preceding paragraph were unable to maintain growth of the protozoon. Organisms A, B, C when tried singly were also unsuitable. Not only did C fail to support growth of the ciliate but if added in overwhelming numbers to a culture of the protozoon on A + B, it actually inhibited multiplication of Euplotes. For the present we have dispensed with it.

We also used a strain of *Escherichia coli* (*B. coli communis*) described here as K_{13}. This organism has received attention by other investigators studying the nutrition of protozoa and for additional reasons which will be apparent later we desired to use it. By itself, in the bran extract medium, we found that growth of the ciliate was fair or poor. Combined with A and B, themselves poor as food for the ciliate, excellent cultures resulted. It should be added that coincident with the use of *B. coli communis* and the five bacteria previously described, we employed a pure line of *Euplotes taylori* started from a single, sterile, individual.

At this stage of the work we learned through parallel studies that a 0.01 per cent solution of glucose in 1:1 ASW was superior to our bran extract medium in 1:1 ASW. With appropriate bacteria present excellent cultures of protozoa resulted. In fact the glucose-containing cultures were so densely populated that the use of the bran extract medium was discontinued. This was also regarded as a step forward in the simplification of media. Below are tabulated the results of the experiments with single strains of bacteria or combinations thereof:

BACTERIA	PROTOZOON GROWTH
A	None
B	None
C	None
Coli	Fair to poor
A(excess) + B	Good
B(excess) + A	None
A + coli	Excellent
A + coli + B(relatively few)	Excellent[1]
A(excess) + coli + B	Excellent

[1] Many of these cultures were more densely populated than any we have ever seen.

We are of the opinion that B contributes little, if any, to the excellence of a culture containing A + B + coli. Further, many successive subcultures have been made to each of which fresh supplies of A and coli have been added but none of B. These subcultures continued to thrive. Finally if cultures containing these three bacterial strains be plated out it is found that most of the colonies are of A, coli is next in abundance, and B is either a decided minority or may even be so reduced in numbers as to escape detection. The latter grows very slowly.

During the introductory experiments we occasionally observed that the highest division rates followed the use of large numbers of protozoa as inocula. This observation supports Robertson's theory of allelocatalysis (33) referred to in the introduction. On the other hand sterile filtrates of thriving cultures when added to mediocre cultures failed to accelerate reproduction. In addition, such a filtrate

was inoculated with A + B + coli and sterile Euplotes introduced. As a control, a fresh 0.01 per cent glucose medium was treated in the same manner and was inoculated with A + B + coli and with the same number of sterile Euplotes from the same stock culture. The number of protozoa which developed in the latter soon decidedly eclipsed the number present in the inoculated filtrate.

The attempted cultivation of Euplotes taylori on media free of living bacteria

Having demonstrated that the ciliate could be grown in a simple basal medium of 0.01 per cent glucose in 1:1 ASW on simple combinations of bacteria we attempted next to replace the latter by bacterial extracts, simple organic nutrients, and dead bacteria. We first sought an answer to the question of whether the bacteria nourish the protozoa through the secretion of substances of value as food to the ciliate. As an outgrowth of the experiments recorded in the preceding paragraph we added sterile Euplotes to a sterile filtrate of a thriving culture. Since bacteria had been present in great numbers in the parent culture from which the filtrate was derived, it was assumed that the hypothetical nutrient substance should be present. There was no multiplication of the protozoa. We then modified this experiment by the use of a flask as culture vessel into which had been inserted an autoclaved cellophane sac. Sterile 0.01 per cent glucose in 1:1 ASW was pipetted into the sac and into the space which separated it from the flask. The inner fluid was inoculated with suspensions of bacteria A and coli. The next day, the outer fluid, supposedly rich in the products of bacterial growth and secretion, was transferred to the regular watch glasses used as culture vessels. It was found incapable either of sustaining the growth of added sterile Euplotes or of stimulating multiplication in a mediocre culture.

It occurred to us next that bacteria on disintegration by autolysis might liberate nutrient substances in a form suitable for maintenance of Euplotes. A heavy suspension of A + coli (in 0.01 per cent glucose in 1:1 ASW) was allowed to autolyze over a 10 day period. Even though every organism was not killed, the products of autolysis proved worthless as food for Euplotes.

One reason for selecting the K_{13} strain of *B. coli communis* for experimentation was that we had at hand through the courtesy of the Department of Bacteriology a very active phage for this strain. The opportunity consequently presented itself of studying lysed organisms as food for protozoa. Preliminary experiments in which coli, as the sole strain of bacteria, gave fair growth of the protozoon, showed that addition of the phage was followed by a failure of growth. The experiment was controlled in the next series by examining the toxicity of Martin's broth alone, and Martin's broth plus phage. The corresponding experimental cultures were in Martin's broth plus phage plus A and coli, and secondly Martin's broth plus A and coli (phage omitted). The results showed clearly that lysis of coli rendered the medium unsuitable for the growth of Euplotes.

MEDIUM	GROWTH OF EUPLOTES
Martin's broth	None
Martin's broth + phage + A + coli	Poor
Martin's broth + A + coli	Good
Martin's broth + phage	None—Evidence of toxicity

Many experiments were conducted in which, with bacteria omitted, attempts were made to grow Euplotes on dissolved

foodstuffs. The following substances were tried without securing any multiplication of the protozoa. In every case 1:1 ASW constituted the inorganic medium to which the experimental substance was added in the concentration indicated: .01 per cent sodium lactate, .01 per cent inositol, .01 per cent glucose, .01 per cent ammonium glycerophosphate, .01 per cent alanine, .01 per cent asparagine, inositol plus ammonium glycerophosphate, glucose plus ammonium glycerophosphate, bran extract plus ammonium glycerophosphate. Furthermore, the addition of *B. coli* in most cases failed to so improve the medium as to permit growth of Euplotes. When *B. coli* was added to sodium lactate and to inositol plus bran extract, slight growth of the ciliate was observed. Inositol was tried because of the identification of it by Eastcott (45) as bios I. The use of sodium lactate, glucose, and ammonium glycerophosphate arose from the work of Peters (24) on *Colpidium colpoda*. Five per cent sterile dilutions of rabbit, guinea pig, and horse sera in 1:1 ASW were also found incapable of supporting the growth of sterile Euplotes. The blood sera themselves were presumably non-toxic since the addition of small quantities (0.1 cc.) to 2 cc. portions of cultures of Euplotes on A + coli in .01 per cent glucose failed to retard reproduction. With horse serum only was there any indication of toxicity. This is in agreement with the work of Oehler (31) who failed to grow protozoa on soluble foodstuffs. Finally we attempted to cultivate Euplotes on dead bacteria. *B. coli* suspended in 1:1 ASW was killed by heating at 60°–65° for 1½ hours. To the suspension was added .01 per cent glucose and sterile Euplotes. No multiplication of the protozoon was observed. In similar fashion organism A, killed by heating for 1½ hour periods on three successive days, failed to support growth. Experiments in which a mixture of the two dead strains was used were unsuccessful.

Ralph Baker, who was associated with us a year ago, attempted the use of toluene-killed bacteria. The toluene was afterwards removed with a current of sterile air. The product failed to support the growth of sterile Euplotes, although as soon as live bacteria were added excellent growth resulted.

Accordingly we have been unable thus far to meet with the success recorded by Tsujitani (7) and Oehler (13, 14) in the use of dead bacteria.

Most recently we have tried, without success, the use of suspensions of disintegrated bacteria, in which the disintegration was effected by exploding with carbon dioxide.

This study, admittedly qualitative, is now being continued on a rigid quantitative basis by numerical counts of both bacteria and Euplotes in the cultures. No mention has been made of pH control. This has been the subject of a separate study the preliminary findings of which demonstrated to us that the extreme limits for growth of Euplotes on mixed bacteria in bran extract were pH 4–9. In our own experiments we have merely endeavored thus far to see that the media employed fell between pH 6 and 8.

Summary

1. The hypotrich, *Euplotes taylori*, has been obtained free of bacteria by repeated washing with sterile artificial sea water.

2. In the presence of suitable bacteria the ciliate grew luxuriantly in a basal medium of 0.01 per cent glucose in diluted artificial sea water.

3. On single strains of bacteria, including *B. coli communis*, and five strains

isolated from a bran extract medium, *Euplotes taylori* grew poorly if at all.

4. On a combination of two of these bacterial strains marked multiplication of Euplotes was observed.

5. Sterile filtrates of thriving cultures, bacterial dialysates, autolyzed bacteria, phage-lysed bacteria, toluene-killed bacteria, and heat-killed bacteria failed to support the growth of Euplotes.

6. Simple nutrient media, free of bacteria, consisting of various carbon and nitrogen compounds in artificial sea water were likewise unsuccessful.

7. Blood serum in artificial sea water gave negative results.

To the Society of the Sigma Xi we are indebted for a generous grant which assisted in the prosecution of this work. We acknowledge also the courteous coöperation of the Department of Bacteriology in the provision of research space, equipment, and technical aid. Professor C. B. Van Niel was good enough to examine the manuscript and advance several helpful suggestions.

Note added Feb. 11, 1931. We now have evidence that *Euplotes taylori* may be reared, under suitable conditions, on the single organism A. This is now recognized as a large, fluorescent, gram-negative bacillus, giving many of the reactions of *Bacillus fluorescens pseudomonas* (Bergey classification).

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NERVE CONDUCTION IN RELATION TO NERVE STRUCTURE

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IT IS historically true in all science that structural knowledge usually precedes functional. In biology, anatomy was far advanced when physiology hardly existed. This is natural enough, since dynamics are more complicated than statics, and since, moreover, the anatomy of a machine may be described with no knowledge of its action while its action is usually meaningless if the structure is not understood. The anatomy may be *described*, but it remains a jumble of parts and dimensions until seen in relation to its function.

In the nervous system, beyond comparison with any other organ, the cell structure and the intercellular connections are so elaborate that even the anatomical facts have been slow to appear. The physiological knowledge is correspondingly very meagre; but enough exists even so to suggest some of the ways in which this complicated structure may be understood in terms of function.

As an indication of the type of correlation possible, it will be recalled that different axons and dendrites in the individual peripheral nerves have variable fibre diameters (96, 127, 128). It is now known that the functioning of a nerve fiber depends in a very direct manner on its diameter and that nerve fibers of larger diameter conduct more rapidly (61), are more easily excited (103, 105), and respond to external influences in different ways than do other fibers of smaller diameter. It has been shown, in fact, that the fiber groups of a given size tend to carry impulses related to definite functions; the large fibers, for example, carry motor and proprioceptive impulses, the smaller ones transmit impulses aroused by pain stimuli (46, 62).

The above does not imply that for every type of sensation or effector action there exists a unique type of nerve fiber. It has been shown histologically that a single sensory fiber may branch and reach end-organs of quite different anatomical character and presumably, therefore, of not identical function (114, 133). Also, there is physiological evidence in the trigeminal nerve, nearly all fibers of which divide on entering the medulla and run to separate nuclei, that touch sensations are relayed only through one nucleus, pain only through the other (63, 140). The separation of impulses carrying these two sensations apparently occurs at the synapses in these two regions.

The purpose of this paper is to indicate some of the relations that can now be stated or surmised between structure and function in nervous tissue, and still more, to point the direction in which further information is needed. Before considering this problem, it is necessary to introduce some of the present knowledge and concepts regarding the nature of conduction in the nerve fiber and across the synapse.

THE ACTION POTENTIAL

To study nervous activity there must be some means of measuring it or, more

accurately, measuring some change accompanying it. For a millenium the only index of the passage of a nerve impulse in a nerve was the twitch of a muscle innervated by some of the fibers in it. Eighty years ago DuBois Raymond (45) discovered a measurable electric change in the nerve itself. If electrodes are placed at two points on the side of an uninjured nerve and connected through a galvanometer, no current flows, showing that the nerve surface has essentially the same electric potential at all points. If now the nerve is cut or crushed under one of the electrodes, the galvanometer at once gives a deflection, as if the two electrodes were connected to a weak battery and the direction shows that the injured end corresponds to the negative pole. This is the injury or demarcation potential of nerve, the injured part becoming negative to all uninjured points, and remaining so while the nerve is at rest. When the nerve becomes active, the galvanometer shows that the potential difference between the normal and injured points becomes, for a moment, less. Since the injured part does not respond to activity, this must mean that the normal nerve becomes less positive or more negative when active. This is the action potential of nerve, a brief potential change at each region as it becomes active, making it more negative than it is at rest before and after the nerve impulse passes it.

The nerve impulse travels in human nerves at rates up to 120 meters per second (85, 86, 126) (about the highest speed ever achieved in an automobile) and the action potential sweeps along at the same rate (20). This and much more evidence shows that the action potential may be used, with some caution, as a quantitative measure of nerve activity. It is also interesting to note for later reference that the surface of the resting nerve becomes less positive both on injury and during activity; in the one case permanently, in the other, temporarily. This suggests that activity may involve the reversible breakdown of a structure (membrane).

Only in the last decade have other changes been discovered in nerve during activity. All tissues studied, except nerve, had been shown to increase their chemical activity when functioning. They use more oxygen to burn more food stuff and produce more carbon dioxide and free more energy, mostly heat. The amount of oxygen used can serve as a measure of the increased activity, as can also the extra heat liberated. These measurements have now been successfully made on nerve (44, 52, 64a, 65, 120, 146) and they show that during activity a nerve does use more oxygen and form more heat and carbon dioxide than when at rest, as well as undergo other chemical changes (72, 73, 74, 88, 89); and these new measures of conduction are being utilized along with the action potentials in the study of nervous function.

CHARACTERISTICS OF NERVE ACTIVITY

Using these methods of study, several important generalizations have been reached concerning nerve activity: 1) the nerve possesses an independent irritability (78); 2) a refractory period appears following the conduction of an impulse, during which the nerve cannot be reactivated (6, 27, 33, 76); 3) anatomical and physiological continuity of the nerve fibers is required for successful conduction (56, 78); 4) the nerve impulse can spread in an individual fiber from the point stimulated in both directions (99), even though normal impulses go only in one; 5) the impulses conducted in a single nerve fiber remain isolated in it and do not spread to other adjacent fibers (56, 78, 98, 148); 6) impulses traveling along a nerve may be

reversibly blocked by the action of various agents (144); 7) the impulse carried by a nerve fiber shows an all or nothing behavior (1, 94, 111, 143)—that is, when conditions are such as to permit a nerve impulse to travel, the maximum impulse possible always is propagated; the only alternative is nothing.

1. Independent irritability. Normally in the body it is doubtful if nerve trunks are ever directly excited, for impulses are transmitted to them from excited end organs or across synapses. The fibers themselves are, however, highly excitable. A rap on the "funny bone" stimulates the ulnar nerve itself. The sciatic nerve of a frog with attached gastrocnemius muscle is easily dissected out and lives for days with proper care. Such a nerve can be stimulated at the central end and a muscle twitch proves that an impulse has travelled the length of the nerve. A variety of agents may serve to elicit this response: mechanical tapping, application of chemicals, heat, and, best of all, electric currents of all sorts. These latter have been quite widely used to study the irritability of nerves, since they can be accurately measured and delicately graded. It thus appears that when a constant current is led through a nerve by two electrodes, the nerve is stimulated at the negative one, cathode, rather than the positive one (125). It is noteworthy that an active region of the nerve becomes negative, and a region made negative becomes active. Further, the stimulating currents must have a minimal or threshold strength to excite, and this threshold is less for long lasting currents than for short ones (a current lasting one-hundredth of a second is relatively long (100)). Roughly, a certain amount of current must flow to excite and, in a liquid conductor like nerve, this means a certain number of ions must move. This number we may, for simplicity, consider constant for any nerve fiber in any particular condition.

2. Refractory Period. The strength of stimulus required to excite a nerve is greatly increased shortly after a nerve has been active. For one to several thousandths of a second after an impulse has passed down a nerve it cannot be excited at all (the absolutely refractory period (111)), then during the next hundredth of a second (the relatively refractory period), it becomes more and more irritable (will respond to a weaker electrical shock) until it has returned to its normal resting condition. This shows that an important change occurs in the nerve when it is active, from which it rapidly recovers. A similar change occurs in the size of the nerve impulse itself; it is less than normal and travels more slowly than normal when started during the relatively refractory period (111). The change during activity thus affects both "irritability" and "conductivity" of nerve, which then recovers during a refractory period of a fraction of a second. As a matter of fact, the heat production (64) and oxygen consumption (65) associated with activity are not completed for ten minutes or more (at 15°C.) so that a nerve has not fully recovered for this time after becoming active. Action potentials also persist for minutes (9, 67), which, with the chemical changes, may be of importance in determining passage over a synapse.

3. Antidromic Conduction. The fact that the nerve impulse travels away from a stimulated point equally well in both directions shows that no pre-existing condition in the nerve determines the direction of propagation, and leads to the conclusion that activity of one place on the nerve is the essential stimulus to neighboring regions.

4. Isolated Conduction. Although activity spreads from point to point along one nerve fiber, it does not jump from one fiber to adjacent ones. If this were not true, it would be impossible to detect as separate sensations the touch of two points close together on the skin, nor to contract a muscle slightly while leaving most of its fibers at rest. It will be seen that this limited spread of activity is highly dependent on the nerve structure.

5. Block. All the agents that can excite a nerve, and many others, are able to block it when applied more intensely. Cutting or crushing a nerve blocks the impulse at the injured region, but such a block is permanent. A block can be produced at any region along a nerve by heat or cold (28, 35), pressure (116), local anesthetics and narcotics (1, 139, 143, 144), asphyxia (14), electric currents (125), etc., and if done carefully there is no permanent injury. When the agent causing block is removed, conduction past the point of block returns. This shows that conduction requires not only anatomical integrity of the nerve fiber but also an easily disturbed physiological balance. All the agents that cause block, when somewhat less intense, cause depression. A nerve impulse cannot pass at all a stretch of nerve exposed to concentrated ether vapor, but a feeble impulse can pass a stretch exposed to dilute ether vapor. This leads to one of the most important generalizations about nerve conduction.

6. The All or Nothing Law. Suppose a nerve passes through a chamber containing dilute ether vapor. It is stimulated at one end and electrodes are placed on the nerve before it enters the chamber, in the chamber, and on the far side, to measure the action potential (and so the intensity of the nerve impulse) at each region. The electrode on the near side indicates the size of the normal impulse. When the impulse passes on into the ether chamber it is decreased, the second electrode shows a smaller action potential than the first. The interesting question is: What happens to the impulse when it passes out again into normal nerve? It might, of course, remain small as it was in the depressed nerve, but it might also, conceivably, return to normal size now that it is again in normal nerve. This is, in fact, what happens; the far electrode shows the same electric change as the near one (42, 94). The size of the nerve impulse in any particular portion of nerve depends, then, only on the condition of that portion of the nerve and not on the previous history of the impulse. This means, in turn, as has also been experimentally shown (3, 4, 113), that a particular nerve fiber under any given set of conditions can carry only one size of impulse, its maximum for those conditions, or none at all. It responds to a stimulus, either from the outside or from an adjacent region of the nerve fiber, with its all or with nothing.

THE NERVE IMPULSE

From these data emerge certain basic characteristics of the nerve impulse, the wave of change that travels along a fiber and evokes activity of muscle, gland or other nerve cell at its end. The impulse can be started by a stimulus, but once started its propagation continues quite independently. If the initial stimulus sets into action only the local nerve region near the electrode, what starts action in the more distant regions? There seems to be only one answer that fits the facts: The activity of one region of the nerve somehow gives the stimulus to the next region, this to the next, and so along.

The impulse has been defined as "a propagated tendency to excite" (42) and

is often likened to a spark burning along a fuse. In this latter case, heat is the agent that starts a chemical change at some point; the reaction liberates enough heat to start the same change in the next region, the heat from this starts a third point, etc. If the initial heat applied (stimulus) will just start the reaction, its further travel goes on automatically. The size of the spark depends only on the fuse in which it travels. If it reaches a damp region, it becomes feebler, or goes out and is blocked; but if not blocked, when it passes on into dry fuse, it flares up to its normal size. In the nerve, also, the stimulus starts a chemical change, and this starts the same change further along, but the means by which the first change brings about the second is not so simple. It does not seem possible that it does so by means of a rise in temperature, for a single impulse raises the temperature of the nerve hardly one ten-millionth of a degree (64). It has been noted, however, that electric currents, or ion changes, easily excite nerve on the one hand, and, on the other, move along it with the impulse. It seems very probable that these currents in the nerve are the means of excitation of a resting region by an active one; and since ion movement is determined by resistances, polarization and the like, which are in turn expressions of structural conditions, it is not surprising to find that the further analysis of conduction in the nerve fiber enters at once into questions of its morphology.

The general view of the nerve impulse now held (41,106) is somewhat as follows. Consider a nerve fiber as consisting of a cylindrical mass of protoplasm surrounded by a (plasma) membrane and lying in tissue fluid. The protoplasmic core contains salts and other ions that can freely move about in it, and the tissue fluid is similar in this respect. The membrane separating them, however, contains few ions and offers great resistance to the passage of ions through it. It has, therefore, a high electrical resistance, and this has been actually determined (127). The material of which the membrane is composed, at least in part, is assumed to be chemically very active so that it breaks down under certain conditions in an explosive fashion. It is also probable that this membrane is polarized at rest with more positive ions on its outer surface and more negative ions on its inner one. When the membrane is broken down, ions are able to pass through and neutralize the inside and outside (see Fig. 1). This explains why an injured part becomes less positive than an uninjured one and why a similar change toward the negative appears at an active region, for the electrodes record the condition at the outer surface of the fiber.

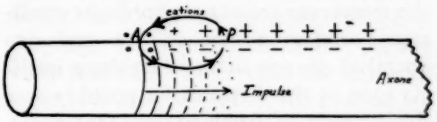

FIG. 1. MODEL OF THE NERVE IMPULSE
For explanation see text

When an electric current is led through a nerve, the electrodes are not on the individual axons but are in contact, through the perineureum, with the tissue lymph or fluid. Positive ions migrate away from the positive pole along the nerve toward the negative pole, and negative ones in the reverse direction. Most of them will move freely in the tissue lymph, but some must come against the nerve fiber membranes. Near the anode, positive ions will move from the fluid against the membrane; near the cathode negative ones will do the same. In the fiber cores ions will also move, positive ones towards the cathode, negative toward

the anode, until they reach the membrane. Near the cathode, then, negative ions move to the outer surface of the membrane from the surrounding fluid and positive ions move to the inner surface from the axon core. The reverse occurs at the anode. The resting membrane, we have decided, is polarized with extra positive charges on the outside and negative within. The applied current, then, will increase the polarization near the anode, but near the cathode new ions which move to the membrane neutralize those already there. At the cathode the membrane is depolarized, and it is here that the nerve impulse starts when stimulated by the applied current.

The next step is largely hypothetical. It is assumed that the depolarization of the membrane somehow affords the condition necessary to set off the explosive chemical change in the membrane itself. As soon as this happens, or possibly as a direct result of depolarization, the resistance to ion movement through the membrane disappears at this point, very much as if the insulation of a wire were scratched off there. Now, quite aside from any current sent into the nerve from the outside, further changes must follow. The membrane next to this active region is still in its resting state, polarized with positive ions outside and negative inside, but they are no longer held apart by an intact resistant membrane. Ion streams are able to pass through the active broken down region close by, and rapidly do so. This, in turn, depolarizes the region of the nerve next to the first one and, of course, the chemical change occurs here and the membrane becomes permeable. In this way, it is obvious, a wave of electric and chemical change must spread along the nerve fiber in both directions from the point first stimulated. This is the nerve impulse, a propagated excitation.

Certain steps in this development are hypothetical, and it must be recognized that the picture has been simplified to a merest skeleton. The action potential, for example, may not represent a passive depolarization but a potential actively produced by the chemical reactions. But whatever the details, it is highly probable that the nerve impulse consists basically of a local membrane change of a chemical and physical nature, which leads to flow of ions, or current, which in turn starts the local membrane change at adjacent points. This accords with all the facts detailed above, and Lillie (106) has happily developed a model which is known to depend on such a mechanism and which transmits "impulses" that conform to practically all the properties of the nerve impulse.

This consists of an iron wire surrounded by a membrane of iron oxide and lying in nitric acid. When current is passed into it, a wave of break-down of this surface film starts at the cathode and travels along the wire accompanied by an action potential. After the membrane is rapidly broken down, in the wire as in the nerve, it reforms more slowly, leading to a refractory period during which a second impulse is transmitted feebly or not at all.

PART II

The structural complications of the situation can now be considered more exactly. A myelinated nerve fiber is not a tube of homogeneous protoplasm with a membrane around it, as has been abundantly demonstrated by histological studies (114). The axis cylinder contains fibrils and axioplasm limited by a membrane, the axiolemma. A questionable periaxial space separates this central cylinder from an investing layer of myelin, surrounded in turn by a sheet of thin nucleated cells of Schwann. The whole

is still further enveloped in fine divisions of the connective tissue framework of the nerve trunk which pass in from the perineureum and form capsules about individual nerve fibers (sheath of Henle) and groups of them. Longitudinally also there is no homogeneity. At intervals of half to several millimeters, at a node of Ranvier, the myelin is discontinuous, the neurilemma or Schwann sheath dips in towards the axon core, and the core itself is markedly constricted by a "thorny collar." The myelin is further broken between the nodes by oblique conical slits (of Schmitt-Lantermann) in which lie coiled fibrillar structures (Golgi-Reznikoff apparatus) and, even where seemingly homogeneous, a laminated and reticular structure has been ascribed to the myelin substance.

How is the flow of ions, on which propagation depends, influenced by the neurofibrils, the periaxial space, the fatty non-conducting myelin with its slits of Lantermann and interruptions at the nodes of Ranvier, the neurilemma, sheath of Henle, etc.? What is the hypothetical membrane—the surface of each fibril, the axiolemma, myelin, Schwann sheath? Most of these questions, of course, cannot be answered, but it will be interesting to examine the evidence on a few specific points.

Though probably of little significance for the normal activity of nerve *in vivo*, the perineurium has been very important in obscuring the properties of the axones in *in vitro* studies. This dense sheath resists the passage through it of ions or molecules. Thus it tends to distort action currents passing from the axones to the recording instrument (26), and to mask the action of potentials applied to stimulate. Recent work (24) makes it probable, for example, that the ordinary failure of a constant current to cause repeated responses of nerve during its passage, which it should do according to the theory outlined, is due to the inert sheath around the nerve. The diffusion of substances between an outside solution and the interaxonal fluid is greatly retarded. Narcotics act on nerve most rapidly where branches perforate the sheath (130). Methylene blue hardly penetrates the whole nerve but stains it rapidly when the sheath is longitudinally slit (51). The same procedure causes a nerve to block in isotonic glucose or potassium chloride solution in a few minutes rather than several hours, owing to more rapid diffusion (51).

NEUROFIBRILS AND FIBRE TYPES

Assuming the normal existence of neurofibrils, at least in invertebrate nerve (30, 41), what evidence bears on the view that they rather than the axis cylinder as a whole represent the conducting units? Histologically, they are seen to cross the region of the nodes unmodified (118) and, possibly, even to cross the synapse (84), whereas the axis cylinder is markedly constricted with reduction of axioplasm at the nodes and similarly where it leaves the cell body (118). The fibrils, it has been claimed, become finer and more numerous as a nerve is fatigued (114), suggesting a functional change; and Peterfi (124) has recently seen fibrils appear in vertebrate nerve while it is active. On the other hand, astrocytes, without evident conducting function, may have marked fibrils (15).

Conduction is supposed to require oxidation of some substance in a membrane. From the heat produced during conduction the number of molecules of food substance oxidized can approximately be calculated. When the area occupied by such molecules is obtained and compared with the area of the axiolemma, it appears that they would

occupy only a minute fraction of it, a twenty-thousandth (44, 71). (Of course exothermic reactions might be partly balanced by endothermic ones.) If only the surface of a few neurofibrils becomes active, a more probable ratio would be obtained.

Still another observation might be explained in terms of neurofibrils. It has been shown in the dog that the nerve impulse traveling up a sensory nerve is delayed 0.00014 second in passing the spinal ganglion (47). Each nerve fiber is connected by a single T branch with its monopolar cell, and it might be assumed that the impulse has to travel along this branch to the cell body and back before proceeding into the cord. At the usual rate of travel this delay would correspond to a detour of 6 mm. each way. The main difficulty in the case of an impulse involving the whole axis cylinder is the refractory period. The branch could carry the impulse to the perikaryon but would then be refractory to its return for very much longer than .0001 second. If, however, neurofibrils carried the impulse there would be no necessary conflict; for each fibril ascending the nerve might turn into the branch, run into the cell, possibly around the nucleus, continue back into the branch and so on up the dorsal root. The impulse would then not have to retrace its path along the fibril and the refractory period would not come into question.

There is, unfortunately, a new difficulty with this explanation, aside from the absence of certain histological evidence as to whether or not the fibrils, like the axon, form a T with only one branch to the cell. If the nerve impulse must indeed follow a path leading into the nerve cell, removal of the cell body should block conduction even though the fiber beyond the T branch remains intact. The experiment was performed last century (21). In a crustacean the ganglion on the nerve supplying an antenna is sufficiently pedunculated to permit its excision, and conduction was reported to remain intact. Also, Steinach (139) observed conduction through spinal ganglia of vertebrates after the cell bodies showed marked histological degeneration due to obstruction of the blood supply.

This leads us to consider some of the evidence against the neurofibrils being the conducting units. The all or nothing behavior of nerve might be equally valid for the entire axon or the individual fibril. For any nerve, however, the number of the all or nothing units would be far greater in the case of the fibrils than the axon. For a very fine nerve, with only a dozen axons, the number of units has been measured by the muscle response (2, 8). Thus a very weak stimulus should excite only the most sensitive unit and give a certain sized twitch, a slightly stronger stimulus would excite the two most sensitive units and give twice the twitch, and so on until all units are stimulated and the maximal twitch observed. Actually the number of units found agrees with the number of entire axons and is far less than the number of fibrils. A similar analysis by action potentials has been made for muscle fibers (2). It might be argued that conduction is none the less in the individual fibrils and that all those in one axon are, even though reaching different muscle fibers, always active together. But another important group of observations cannot be easily reconciled with this suggestion.

The threshold of any one axon in a nerve trunk, the rate at which it conducts an impulse, and other properties have been shown, as mentioned earlier, to depend on the diameter of the fiber. A fiber with a diameter of 18μ transmits an impulse twice as rapidly as one of 9μ and three times as rapidly as one of 6μ. (This relationship does not hold for still smaller fibers (49)). This has been established by studying the

shape of the action potential in different nerves and at different distances from the point stimulated. As the distance over which the impulse has travelled is increased, the action potential in those fibers transmitting at a rapid rate will be a little ahead of that in the slower ones, and by careful study the actual rate of conduction in different fiber groups can be accurately determined. These are known to differ from one type of nerve to another, and histological examination of these nerves permits counts and measurements of the individual axons to be made. A comparison of the two sets of data gave the results stated (Gasser and Erlanger (46, 62)).

It thus appears that nerve conduction is, over a considerable range, a simple function of axon diameter. This would rule out the fibrils if the large axis cylinder differs from the small simply in the number of fibrils it contains. If it could be shown, however, that the individual fibrils vary in size as does the entire cylinder, the possibility of their acting as conductors would remain. There is another way, also, in which these facts might be interpreted in terms of fibrillar conduction. An examination of the way in which diameter affects conduction rate is first necessary. Before pursuing this subject it will be interesting to see other ways in which this morphological-physiological correlation is likely to be extremely valuable.

The ventral roots of spinal nerves consist almost entirely of large fibers; the dorsal roots mostly of smaller ones of varying size (46, 96). This would suggest that the large fibers with more rapid conduction and with lower thresholds are essentially motor in nature, leading to contraction of muscles, which accounts for the experimental fact that when mixed nerves are stimulated in humans, muscle twitches can be obtained at intensities of excitation too low to cause sensation.

The dorsal root contains a few large fibers, many medium sized and many fine fibers (46, 96). The largest fibers are distributed through muscular branches of the nerve and are proprioceptive in function. The medium sized ones carry impulses leading to sensations of touch and temperature, the latter nerve fibers being somewhat smaller, and the smallest carry impulses which reach consciousness as pain. These facts have been established by the use of different types of nerve block (62). Thus, for example, it is known from clinical experience and animal experimentation that cocaine abolishes conduction in peripheral nerve in the order: pain, temperature, touch (147), whereas pressure abolishes the ability to receive these sensations in the reverse order (87). Applying these methods of block to isolated nerves and studying the action potentials, it is found that the slowest impulses, representing the smallest fibres, disappear first under the action of cocain and last under the influence of pressure.

A similar analysis of fiber groups in terms of function is being pursued into the white and gray rami communicantes of the sympathetic system and into the various sympathetic nerve trunks in the body, as the splanchnic and vagus (parasympathetic) (49, 82). In this latter, at least seven types of fibers are present and it is only a matter of further experimentation to assign to each type one or more of the many activities mediated through the vagus. It has just been reported, for example, that all heavily medullated fibres are somatic, afferent and efferent, the relatively thinly medullated ones are visceral afferent, and the very thinly medullated and non-medullated ones are visceral efferent (81). Obviously, a great field is opened up in the analysis of the functional components of nerves in terms of their fiber population, and with this added clue, nerve connections and patterns in the central nervous

system may be considerably further elucidated.

Returning to our schematic picture of a cylindrical core, surrounding membrane and outside fluid, what determines the rate of propagation? Consider a point (*P*) on the resting membrane a short distance from an active point (*A*) (Fig. 1). *P* becomes active when a certain change in ion concentration has developed there. Ions migrate to or from *P* under the influence of a potential difference between active and resting points. But the number of ions moving across any section determines the current flowing and, for any given potential, this current varies inversely as the resistance of the path it must follow. The path of positive ions, as has been developed, is from *P* through the outside fluid to *A* and from *A* through the inner core to *P*. Finally, it will be recalled that the resistance of any conductor increases as its length increases and decreases as its cross section increases. We now have an explanation at hand for the relation of axon diameter and conduction rate. The speed of conduction will be greater or less as it requires a shorter or longer time for *P* to become active after *A* is active, or conversely as a point, *P*, further from or nearer to *A* becomes active in a given time. This in turn depends on the time necessary for a definite number of ions, or a given amount of current, to flow between *A* and *P*; and, since the number of ions flowing varies inversely as the resistance, this becomes a determining factor. When the sum of the outer resistance between *P* and *A* and the inner one between *A* and *P* becomes twice as great, ions will move at half the speed, the needed number will accumulate in twice the time and the rate of conduction will be halved.

In the case of the large fiber versus the small, considering the axiolemma as the membrane involved, the outside resistance through the abundant tissue fluid may be assumed to be low (see later, however), while that of the core is large. The greater the diameter, the lower the core resistance, then, and the faster the conduction. It might seem at first that, since the cross-section and resistance vary as the square of the diameter, the rate of conduction should also do so. But the membrane area increases with the core diameter and, in a manner of speaking, each portion of the membrane shares the conducting core with all the other portions, so the greater membrane area (varying as the first power of the radius) partly offsets the increased conductivity (varying as the square of the radius).

What would be the situation if the fibrils were the conducting units? Then their cores (assuming that they have a fluid core surrounded by a membrane, which is very doubtful if they are of micellar nature (123)) would be the inside resistance and the axioplasm the external resistance. If the inside resistance were the main one, then variation in fibril diameter would act as variation in axon diameter in the case just considered; and if fibril diameter and axon diameter varied together, it would be impossible to decide which was the conducting unit. On the other hand, if the fibrils had a low core resistance compared to that of the axioplasm (which is not likely since their cross section is so much smaller), a new possibility arises. The conduction rate would then depend on the axioplasm, now the external resistance, available for each fibril. One axon of twice the diameter of another, and therefore four times the area, would conduct at the same rate as the second if it also had four times as many neurofibrils, since the axioplasm for each would not be changed, but four times as fast if it had the same number of fibrils and four times as much axioplasm (one-

fourth the outside resistance) for each. Obviously, we are back to a cytological question: how does the number and size of the neurofibrils vary with the diameter of the axis cylinder?

Another point may be mentioned before leaving the fibril question. The nerve in the foot of a large slug is very extensible. The time required for an impulse to pass along the nerve when shortened was found (36, 92) to be less than when the nerve was stretched. This precludes conduction in a solid structure that might be coiled or extended, since the distance the impulse must travel would then be the same for any position. Of course, the neurofibrils are not now regarded as such inextensible solids.

As will be seen from the evidence considered above, it seems unlikely that the neurofibrils represent the true conducting units of the nerve cell; and certainly non-fibrillar cells, as the fertilized sea-urchin egg, show membrane transmission. It must be kept in mind, however, in considering the relation of diameter to fiber activity that no fiber has a uniform diameter. The axis cylinder is much constricted at each node and near the cell body and is usually quite irregular near an end organ or synapse, and it is claimed (22) that local compression of a nerve does not block conduction when the perifibrillar substance had been squeezed to 1/600th its normal cross-section providing the fibrils retain their normal staining properties. The fibrils presumably are more uniform throughout. Some further considerations of the diameter-conduction relation will be mentioned later. Physiologists have quite regularly assumed that the axis cylinder as a whole is the fundamental unit of conduction. Histologists have been more divided, some, impressed by the anatomical availability of the fibrils, having leaned more to the view that conduction occurs along them. Bethe (22), for example, attributed conduction entirely to the fibrils, the remainder of the cell serving a "trophic" function. The recent, exactly opposite, suggestion of Parker (121), that the fibrils carry nutritive influences is at present purely speculative, and an older idea of their serving as a supporting skeleton is hardly tenable (75). A final answer is, obviously, not yet at hand, and equally obviously, cannot be obtained by either the morphologic or functional approach alone, but only by a proper utilization of both together.

THE RÔLE OF MYELIN

The relation of myelin to nerve function has been a matter of even greater uncertainty than that of the fibrils, and the significance of the nodes of Ranvier has been particularly elusive. Myelin is composed of fat-like material which is very little ionized and a correspondingly poor electric conductor. The suggestion at once comes to mind that the highly resistant membrane needed for propagation of the nerve impulse is the myelin sheath. This cannot be the general case, however, for non-medullated nerves conduct perfectly well. Indeed, it is now fairly certain that fibers normally myelinated can conduct while lacking their myelin, as is the case in late embryonic development (10) or during regeneration. Thus, the longitudinal tracts in the rat's spinal cord are not yet myelinated at birth, but stimulation of the tail evokes responses by the head (70).

Another obvious suggestion is that the myelin acts as an insulator to the axis cylinder and prevents action currents from one fiber from stimulating adjacent ones. That some effective insulation does exist is shown by the fact of isolated conduction previously discussed. But isolation of impulses is also the case in unmyelinated

nerve bundles, though probably not so perfect in these. It may be of significance in this connection that as fibers approach their peripheral endings where, instead of conduction, reaction with other tissues is important, the myelin is invariably lost; and the same is true where fibers meet other nerve fibers or nerve cells, as in the grey cortex or other regions of neuropil (114).

The rôle of the myelin should be most directly suggested by a comparison of the behavior of medullated and non-medullated nerves. One striking difference is in conduction rate, which is much greater in medullated nerves. The non-myelinated fibers are smaller in diameter than the axis cylinder of most myelinated fibers, but the difference in speed of conduction is more than would be expected on this basis (49). How might myelin affect the rate of passage of the nerve impulse?

It was assumed in the discussion of the influence of fiber diameter on conduction rate that the resistance outside of the membrane (we will assume this to be the axiolemma) was low because of the large amount of tissue lymph present. If this resistance were increased conduction must become slower. But plastering an axis cylinder with a good layer of resistant myelin must certainly insulate it to a marked degree from the tissue fluid. The outside current between the resting and active points of the membrane must then flow in the minute periaxial space or through the openings in the myelin to and from the tissue spaces. In either case it might be expected that conduction would be greatly slowed in the medullated fibers, whereas the reverse is the case. Another structural fact enters, however, in the existence of the nodes (and incisions of Lantermann) and this greatly changes the conditions of current flow.

In the bare membrane considered before, when point *A* is active current flows between it and point *P*, as discussed; but it also flows to a greater or lesser extent to a great many other points nearer to or farther from *A*. It was merely convenient to consider a single point *P* in the discussion; actually a large area of the resting membrane is involved in the ion movements, which are consequently rather diffuse. With myelin insulating most of the membrane but with naked axis cylinder exposed at the nodes, the ion flow would be more nearly as in the diagrammatic case and the action would be concentrated at the exposed points. It is conceivable that this would result in the excitation of a more distant resting point by an active one, and that the nerve impulse would, in a sense, jump from node to node. Lillie (110) has, in fact, demonstrated something of this nature with the iron wire model. The wire lying free in nitric acid conducts rapidly. When it is surrounded by a glass tube it conducts more slowly, and the smaller the tube diameter, the slower the conduction. This agrees well with the influence of axon diameter in the nerve itself. If, now, a narrow glass tube running the length of the wire and causing very slow conduction is broken across at several points, thus simulating the nodes in the myelin sheath, the conduction becomes more rapid than when no tube is present and the activation can be seen to jump from node to node.

If such a mechanism does operate in medullated nerves, it is obviously of great importance to know in much greater detail than at present the distribution of the nodes of Ranvier. It is highly interesting that a direct relation does exist between internode length and axon diameter (in large frogs, for example, 7μ fibers have an average internode length of 1050μ; 14μ fibers, of 2000μ (29, 79, 145)), and it is not impossible that the apparent relation between diameter and conduction rate is

really one between rate and internode length. This length increases faster than diameter as the frog grows larger (79), and, for a given sciatic nerve, may be as much as 30 per cent greater in the lower portion than in the upper (79). Careful measurements of conduction velocities being made on comparable material should help decide between the two possible mechanisms. Certainly, as the thickness of the myelin sheath becomes less from one fiber type to another, conduction rate decreases more than could be accounted for by any diameter change. If the stimulating action currents are in fact effective from node to node, the constriction of the axis cylinder with reduction of axioplasm at just these points would render the neurofibrils especially open to activation by them. The thorny collar and transverse plate described at the nodes (118) and in relation to the fibrils would acquire an important functional significance.

It may also be noted in passing that different nerves regenerate after injury at different rates (0.5–2 or more mm. per day). Since the neurilemma appears to enter into regeneration (though not indispensable for it) and there is one Schwann nucleus per node, node counts on various nerves might provide an understanding of these differences.

In the central nervous system, myelinated nerve fibers have no nodes of Ranvier (129) or, according to others (23), nodes at very short intervals. In either case they should conduct at relatively slow rates. The division of axons and dendrites into fine terminal branches should act in the same direction. In all reflex responses, when the time between stimulus and action is determined, there appears a considerable interval beyond that needed for conduction through peripheral nerves to and from the spinal cord and for the effector organ to begin its activity (54, 93). (Beritoff (19) has recently questioned this). This interval is assumed to be the time required for the nerve impulse to pass over one or more synapses. It is not impossible, however, that a large portion of it is due to slow conduction along intraspinal nerve fibers.

During ether or chloroform narcosis of a nerve the myelin swells and irregularly decreases the diameter of the axis cylinder (104). This may explain, in some part, the slowed conduction and depressed responses obtained from a partially anesthetized nerve. Similarly, polarization by a constant current causes, by electro-endosmosis, decreased fiber diameter at the anode and increase at the cathode (13, 135), and conduction rate is altered in the same sense (25).

Another difference between nerves with and without myelin is related to their metabolism. It is generally true that non-medullated nerves fatigue more easily than medullated ones (59, 107). The idea that myelin may serve as a food reserve for the active axis cylinder is an old one, but far from demonstrated. It is now known that nerves do not burn sugar for the extra energy used in activity (89), and changes in phosphorus combination in the nerves suggests that they may burn phospholipins (74). A change in myelin structure accompanying brief activity of a nerve has been reported (13, 95, 142). Also, the appearance of the myelin, as studied under polarized light, alters when a current is passed through a nerve; and a lecithin emulsion can be made to show similar effects (138). When studied in the dark field changes in salt content of the bathing fluid cause rapid alteration of the appearance of the myelin. Salts and polarizing currents may have an interdependent effect on nerve conduction as well as on its staining properties; though the latter is affected only by much more severe treatment (95, 135). Finally, it is well known that

myelin shows marked histological and chemical changes during ordinary degeneration and regeneration of nerve (90, 117). But these problems lead too far into nerve metabolism to be followed here.

It appears, then, that the presence of myelin, and particularly its segmentation, must lead to changes in the electric circuits through and around nerve fibers. If conduction of the nerve impulse depends, as is believed, on the flow of currents, the myelin sheath must exert a profound influence upon conduction, though possibly not in the manner suggested above. Besides a physical effect, there is the further possibility that the lipins of the myelin may play a rôle in the chemical sequence of nerve activity; and this problem is being further investigated.

PART III

PROPERTIES OF THE REFLEX ARC

We have so far considered only the conduction of the nerve impulse along an essentially uniform, unbranched nerve fiber. This is the simplest case, and, therefore, the most studied, but it is obvious that the properties of peripheral nerves are not identical with those of the whole nervous system, or even of the simple reflex arc.

The reflex arc shows many new properties or at least very great quantitative changes in those of the nerve (58, 130). For example:

1. *Fatigue.* Although the nerve fiber is fatigued with difficulty and in myelinated fibers at least never to inactivity (30, 68), fatigue of reflexes is rapid and marked in many cases (69).

2. *Drug Action.* The nerve fiber can be blocked by the various narcotic drugs when they are present in sufficient concentration; the amount necessary to produce an effect on the peripheral nerve, however, is often hundreds of times as much as that needed to abolish reflexes. Strychnin, morphin, caffein, and the like, all will act on the nerve fiber in sufficiently great doses, but as ordinarily used in pharmacological or therapeutic work, their action on the central nervous system is manifested in amounts incomparably less.

3. *Irreversibility.* Whereas the nerve fiber conducts equally in both directions, conduction in the reflex arc is unidirectional; activity passes freely from the sensory nerve into the central nervous system and out by the motor, but stimulation of the central end of the motor nerve leads to no activity of the sensory one (18, 112).

4. *Variability.* The single nerve fiber responds in the most invariable manner possible, all or none. Although the *all* is dependent on the condition of the fiber and, therefore, can be modified by various agents, the amount of variation is negligible under conditions even approximating those in the body; the nerve impulse is therefore practically constant in any fiber. Not so the reflex response. The latent period between stimulus and response, the intensity of response to a given stimulus, even the appearance or non-appearance or the type of response, are all subject to great variation with differing conditions of the central nervous system.

5. *Latent Period and After Discharge.* The nerve fiber begins activity within five hundred thousandths of a second after a stimulus is given (48), and stops as soon as stimulation is over. A reflex response may appear some seconds after the stimulus has been given and, conversely, after stimulation stops the response may continue for some time.

6. *Summation.* If one or a few closely spaced stimuli to a nerve fiber do not excite it, further repetition of the same stimulus will not do so. A reflex response will sometimes follow hundreds of repetitions

of a stimulus which in any shorter sequence would remain ineffective. There is a marked summation of stimuli.

7. *Inhibition.* The converse of this is also commonly seen in the reflex, but only under very special conditions in the nerve fiber. Impulses reaching the central nervous system by certain nerves are able to inhibit reflex responses produced by other nerves at the same time.

8. *Independent Rhythm.* The nerve fiber ordinarily responds to each stimulus given with one response as long as the stimuli are spaced sufficiently far apart so as not to encroach on its absolutely refractory period. It is thus able to respond with 500 or more impulses a second. In the reflex, the rhythm of response is rarely closely related to the rhythm of the stimulus, although in certain types the response may follow frequencies up to 100 a second or more (39, 40, 58, 108).

Since these new properties appear in the central nervous system, it has been natural to look for their explanation in some structure or mechanism not present in the peripheral nerve. The region of junction between two nerve fibers is obviously a new feature and must involve some differences in behavior, so that these properties are usually credited to the synapse itself. The discussion to follow will assume that this is the case, though, in fact, it is not at all certain that many of them are not due rather to interposition of cell bodies and dendrites. For example, greater fatiguability and susceptibility to drugs would be expected in a region with a higher metabolic activity. The gray matter of the central nervous system has a metabolism at least seventy times as intense as that of the nerve fibers (66, 115, 134), so that if the latter would require three hours to asphyxiate, the nerve centers should require only about three minutes. A recent observation that antidromic impulses along motor fibres cause histological changes in their cell bodies while not acting on the synapsing neurone suggests, however, that the point of block is at least on the dendrite side of the cell body (80).

There have been described many types of synaptic connections between axons and dendrites (114). An axon and dendrite may meet simply tip to tip, or may run parallel and in contact for a considerable distance. An axon may twine about a dendrite, end as a knob or plate on a dendrite or cell body, or one or more axones may form a complicated network with dendrites, even to the extent of producing a well defined glomerulus surrounded by a connective tissue capsule. Fibrils may pass across the boundaries of the processes, at least in certain preparations, or not, and all degrees of intimacy of connections have been seen. There are also many physiological types of reflex arcs. The existence of any correlation between functional and anatomical types of reflex connections has not yet been demonstrated, though it may be assumed to exist.

The different kinds of reflexes may be demonstrated in a dog with its spinal cord cut in the thoracic region (136). Among the many reflexes of the legs of such an animal are: the flexion reflex, a pulling away of the leg from a painful stimulus on the foot; and the crossed extension reflex, a stretching out of the opposite leg at the same time. These two reflexes behave very differently in regard to latent period, summation, after discharge, and many other points (58). The flexion reflex appears fully formed in response to a single stimulus; the muscle contraction rate will follow the rate of stimulation up to one or two hundred a second and as soon as the sensory stimulus is stopped, the leg relaxes. The crossed extension reflex does not appear so easily in response to stimulation and can almost never be elicited with

any force by a single excitation. It grows progressively, owing to summation as the afferent impulses are repeated, persists long after they are stopped, and is easily inhibited by still other afferent activity. In the flexion reflex, when the leg flexors contract, the extensors of the same leg simultaneously relax. In the crossed extension reflex, similarly, while the extensors are contracted, the flexors are relaxed. Instead of stimulating the skin of a leg to produce these effects, the afferent nerve from that skin region may be used. Thus, stimulation of the popliteal nerve on the right side will lead to contraction of the flexor muscles on the right side and the extensor muscles on the left side, and relaxation of extensors on the right side and flexors on the left, while stimulation of the left popliteal does exactly the reverse.

It will thus be seen that somewhere in the connections of the afferent neurons with the efferent, there are mechanisms permitting a single afferent fiber to produce motor discharges of a certain type on one side of the cord, of a different type on the opposite side and inhibition of the activity of other motor neurons on both sides.

PHYSIOLOGICAL MECHANISMS OF THE SYNAPSE

The attempt was made for many years to account for these additional properties of the reflex arc by a sufficiently intricate set of connections, having only the known properties of the nerve impulse in the peripheral fiber (111). In recent years this attempt has been largely forsaken as futile and new physiological mechanisms are now assumed to come into play across the synapse. There appear to be two main ways in which a nerve impulse travelling along an axon can initiate activity of an adjacent dendrite and start a similar nerve impulse in it. Either the same kind of ion migration and chemical response which represents successive activation of one region of the nerve fibre by another must also take place at the synapse, or it is conceivable that the end of the axon acts as a miniature gland and, when stimulated, produces some chemical which is able to excite an adjacent or neighboring dendrite.

An interpretation of central inhibition, summation, and other properties has been offered mainly in terms of the second concept by Sherrington (137). Thus, if one impulse travelling over one axon produces a given amount of exciting substance, two impulses over one axon, or one over two, should give twice the amount. If all this substance becomes effective on a dendrite of a second cell, then stimulation of more afferent fibers or more frequent stimulation of the same afferent fibers should have greater effect. This is exactly what happens, the latent period being decreased and the number of responding motor cells increased under either of these two conditions. Also, if a large amount of excitatory substance has accumulated by repeated or intense stimulation, it will take some time for it to disappear, and during this time the motor discharge should continue. If certain types of axon endings produce excitatory substances or changes, other types of endings might equally well produce inhibitory substances which tend to neutralize the excitatory, the two summing algebraically. The correct prediction may be made that if the right and left perineal nerves are stimulated at the same time, since one tends to excite the flexors of the right leg and the other to inhibit them, the result actually obtained may be nil. (More commonly, alternate stepping results—which is less simply interpreted.) It is certainly of importance in this connection that there are morphologically different synapses made by various axons in connection with a single cell (16), so that the possibility of different end-effects by

these axons is at least histologically justified.

For this view it is not particularly important whether a membrane, separating the two cells at the synapse, is present or not; although the former condition is more or less implicitly assumed. Even for the more physical interpretations of conduction across a synapse, the presence or absence of a membrane similar to that around the fiber is not of vital importance. It will be readily seen, in terms of the previous discussion, that a transmitted membrane change, which constitutes the nerve impulse, might quite easily involve a membrane separating two cell processes, so that it would actually help in the transmission of the impulse across the boundary.

The physical interpretations of synaptic conduction depend in more detail on the known properties of conduction in nerve fibers. Thus, it will be recalled that a fiber of large diameter has a lower threshold and reacts more rapidly than a smaller fiber. It is quite conceivable, then, that if processes of small and large diameter were in contact, or even in continuity, that an impulse travelling along the small fiber might successfully pass on into the large, which has a lower threshold, whereas the reverse might not be true. The junction of a fine and coarse fiber, then, would account very simply for irreversible conduction in the synapse (53). Further, any two fibers of different thresholds—that is, requiring electrical currents of different intensities and durations to activate them—might not be able to stimulate one another. If these characteristics of excitability were modified, new patterns of response would result. Bremer (34) has found that the afferent fibers of a spinal nerve have a threshold quite similar to the efferent fibers going to flexor muscles, whereas the fibers to extensor muscles have a quite different threshold. Under the action of strychnin, all thresholds are lowered and become similar. The result is that the afferent impulses normally producing contraction of the flexors only now lead to contraction of flexors and extensors together, and a general muscular spasm results. A similar relationship between threshold of nerve and of the muscle to which it goes has been elaborated by Lapicque (101, 102), who explains the action of certain paralyzing drugs, such as curare, in terms of their ability to change the threshold of one tissue and not the other. (This has been seriously questioned by Rushton, 132.)

As further evidence on the question of irreciprocal conduction in the synapse, some recent work (12) has shown that such conduction may be established in tissues where there is unquestionably protoplasmic continuity. If a sartorius muscle, with parallel fibers running nearly its whole length, is stimulated at either end the excitation is transmitted the whole length of the fiber and it all contracts. If the muscle is compressed by a horizontal surface in the center, conduction from either end is blocked at the same time. If, however, it is compressed at the center by a tilted surface, so that the pressure at one side is established sharply and at the other side gradually, it is found that conduction is blocked in going from the normal region to the compressed one across the line of sharp compression, but not blocked when going in the other direction. Again, it is known that in the coelenterates conduction is possible in any direction along the nerves, which were long regarded as a true net or syncytium (119). Recent evidence (31) indicates that even in these animals there exist many synapses between the individual neurons, but axons and dendrites are morphologically quite similar. It would seem that the presence or absence of a transverse synaptic membrane is quite immaterial; as long as the nerve processes

meeting each other at this point are alike in structure the impulse may travel from either one to the other. In the vertebrate nervous system, where irreversible conduction is the rule, there is usually a marked difference between the axon and dendrite meeting each other in the ordinary type of synapse; the axon being normally thin and fairly smooth, the dendrite thick and thorny (23, 83). In such an arrangement, the nerve impulse might be expected to go from the thin to the thick fiber but not in the reverse direction.

It must be noted that the chemical and physical theories together account for all the major properties of reflex conduction, but neither one alone is able to do so satisfactorily. The physical theory, especially, had difficulty in accounting for delayed and prolonged motor effects, since the stimuli involved are all action potentials of short duration. The recent findings (67) that these potentials may last for minutes may remove some of these difficulties.

Conduction from sensory ending to nerve fiber or from nerve fiber to effector also involves the transmission of excitation across a cell junction. It has usually been assumed that similar relations hold in these transmission regions as in a synapse. The particular complex structures of the different types of sensory endings cannot yet be successfully related to their specific functions, but certain characteristics common to them all cannot be without significance. Thus, in all cases, the nerve fiber loses its myelin sheath at a greater or lesser distance from the end organ, and in the end organ proper the simple round axis cylinder may undergo a bewildering variety of divisions, coilings, swellings and the like (114). Common to all these is the establishment of a relatively large surface at the receptive end of a fiber. This increased surface must lead, in terms of our concept of nerve excitation, to a great reduction in the threshold for excitation, and it is in just such a lowering of threshold that the end organs express their function. In the case of the end organs, as in that of the synapse, it does not appear difficult to understand transmission, whether or not a membrane is interposed between two reacting cells. The epilemmal and hypolemmal endings in muscle would correspond roughly to synapses with and without interposed membranes, yet there is little doubt that in both cases transmission across the boundary is easily possible.

The definite assignment to specific types of sensory endings of the reception of particular sensations is not yet complete, but a very effective start has recently been made (3, 4, 17). It has been shown, for example, by vital staining of the human conjunctiva that the Krause end-bulbs receive cold sensation (141). Also, it may be pointed out that there is no difficulty in reconciling the all-or-none law for the nerve fiber with the ability to sense gradations of stimuli; for a weak painful stimulus produces a slow succession of impulses in the afferent nerve, whereas a strong stimulus produces more frequent impulses of exactly the same character (3). Here, again, the chemical views of transmission across junctions are useful in interpreting the results. A weak stimulus produces a moderate change which in turn generates few impulses; a stronger stimulus produces a greater change and more rapid discharge.

EXTRA-REFLEX EFFECTS

As it was found with the advance of knowledge that no degree of complication of the properties of the axon would adequately account for the properties of the reflex arc, so it seems not unlikely that the reflex arc is not an adequate mechanism to account for all the phenomena exhibited by the central nervous system. Some other means of influence of one part of the nerv-

ous system by another than in terms of nerve impulses conducted between them is suggested by many facts. For example, the establishment of new reflex paths is itself difficult to explain with our present conceptions. Conditioned reflexes, which are easily established, have been widely studied (122). A dog's salivary gland will secrete as a reflex response to the presence of food in the mouth. This is true for all normal dogs and does not depend on the previous experience of the individual. It is an unconditioned inherited reflex. No normal dog secretes saliva when a bell vibrating a particular note is sounded, but if a dog is fed a number of times just after hearing this particular bell, there is established a new reflex so that the ringing of the bell is now an adequate stimulus to salivation. This is the conditioned reflex. Obviously, some type of nervous connection between the auditory center and the salivatory nuclei has been established. Since the individual neuron presumably responds in all or none fashion, so that the impulse travelling in any part of it is uninfluenced by its own history, it is hardly conceivable that it should be influenced by its future. That is, auditory impulses coming along the cochlear nerve and ascending in the central nervous system cannot change their path so as to connect with the salivatory centers, or change potential connections to effective ones, simply because these are active, unless there is some new type of influence exerted by the active centers.

Again, there is often seen the histological picture of the connection of many axons with several widely branched dendrites of a single cell (114). The presumption is that these may all simultaneously affect the common cell and there is physiological evidence, in many cases at least, that their effects may be summed. The case of the mitral cell and the glomeruli in the olfactory system (114), where thousands of fibers reaching a glomerulus are represented by one leaving it, may be mentioned. On the basis of a chemical or an electrical transmission from the telodendrion of one axon to the particular dendrite in its neighborhood, the response of the cell as a unit to the summed action of many axons on separate dendrites cannot easily be explained.

A still more striking indication of the limitations of the simple reflex concept is seen in the synchronous discharge of groups of nerve cells. In the retina, for example, with millions of receptive endings and of conducting fibers, there exists very sharp discrimination. An object whose image falls on a group of cones can be recognized in consciousness in terms of the number and position of the cones stimulated. If electrodes are placed on the optic nerve while connected with the retina and luminous objects of any size or shape are placed in front of the eye, the activity of the various nerve fibers can be observed in terms of action potentials (7). When a few fibers are excited by a small object each one sends out a series of rhythmical impulses quite independent, in time, of the discharges of any other nerve fiber, so that the total effect is an irregular electrical hodge-podge of potential changes. When a great many fibers are excited by a large object, again each one discharges at its own tempo, and this remains true when nearly all of the retina is illuminated, with only a small darkened region left. When, however, the entire retina is evenly illuminated there suddenly appears a new effect. The individual fibers are no longer carrying impulses at independent rates and times, but the whole group rapidly falls into line so that the discharge in thousands of fibers is timed as if it were one (7, 57). This synchronism is so exact that it is difficult to believe nerve impulses travelling over connecting fibers (which might

conceivably carry to all cells simultaneously the stimulus to discharge) would reach all at once, and even if they did, the absence of synchronism when less than all is illuminated is then impossible of explanation. During respiration, impulses originating in the respiratory center travel down the thousands of fibers in the phrenic nerve and produce a contraction of the diaphragm. Here it is found that during deep inspiration the impulses in all fibers are timed together, so that the nerve cells in the center must have discharged together as a multiple unit (5, 60).

Other evidence comes from the psychological field. An acquired response to a particular stimulus pattern is not dependent on the actual sense organs stimulated and their central connections (97, 106). A complicated figure seen only with one eye is at once recognized and responded to when seen with the other. Lashley (106) has found that the ability of rats to learn or retain successful maze habits depends on the mass of the cerebral cortex. Destruction of brain tissue leads to loss of ability proportional to the extent of the injury. Extensive linear cuts causing little actual loss of tissue but great interference with conduction paths, on the contrary, have little effect. Learning thus appears to depend on some kind of mass integration of the activity of large numbers of neurones; and, of course, all normal subjective experience indicates a unity which is apparently inexplicable in terms of separate impulses rushing along innumerable fibers from cell to cell of the brain.

Finally Coghill's (38) work on amblystoma larvae, showing, during development, the successive crystallization of unit reflexes out of a homogeneous response background is in line with the above mentioned material.

It is not yet known what type of mechanism, aside from the passage of nerve impulses, may be held responsible for these phenomena, but the possibility certainly exists that regional potential changes enter into it. It will be recalled that an active cell develops a negative potential in relation to resting regions; this is true for the nerve fiber and, possibly, for the nerve cell to a greater degree. Also, the sensitivity to stimulation and the type of response of a nerve fiber can be modified by passing electric currents through it, quite aside from their ability to excite it directly (25, 125). In the cases discussed it will be seen that the activity of a large number of cells at approximately the same time would produce potential changes of a whole region which, in turn, might modify the sensitivity of other cells and tend to bring the entire group into synchrony.

There is at least one other situation in regard to the nervous system where potential differences seem to play a morphologic rôle. The processes of the neuroblasts, during the original histogenesis of the nervous system, grow in quite different directions and, in general, seem to develop towards actively growing regions of the body. The expression "neurobiotaxis" has been used to designate this phenomenon (11), which resolves itself essentially into the tendency of nerve fibers to grow in the direction of a negative potential (37, 91).

These, then, are a few indications of how nerve function may be viewed in terms of nerve structure and what the structure may mean functionally. It must be recognized that many of the relations suggested, especially in the second and third parts of this paper, are pure (though not gratuitous) hypotheses. They may all be quite incorrect. The purpose in presenting them is largely to stimulate inquiry and to give meaning to some of the, superficially unimportant, structural details of nerve. Only by the simultaneous pursuit of struc-

tural and functional facts and their close correlation will many of the problems raised here be finally answered.

This article is the outgrowth of an effort to indicate to students of histology the functional significance of nerve structure, as described in Maximow's Histology. This was originally requested by Professors W. Bloom and C. J. Herrick, editors. Literature since April, 1930, when this article was submitted, is not considered, though certain references have been brought up to date.

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FACTS AND THEORIES OF BIRD FLIGHT

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BESIDES the birds and their immediate ancestors, only certain insects and bats have succeeded in solving the problems of true flight. Many other forms, having derived sufficient momentum from another medium, can glide through the air for a considerable distance. True flight adds to this the ability of maintaining both altitude and speed by displacement of the air itself. Much has been written of the origin of bird flight but little is definitely known. It may be that it developed from the gliding leaps of the tree-living ancestors of the modern bird. Certain amphibians and mammals incapable of true flight but capable of gliding have been observed to terminate long glides with an upward turn. This sudden gain of altitude takes them up to a selected landing place, but at the cost of their momentum. It is quite conceivable that a successful glider would lengthen the span of flights by vigorous downward displacement of the air with movements of its gliding surfaces. The more generally accepted notion, however, is that the original flyers launched themselves into the air not from treetops but from the ground. It is assumed that these forms were capable of rapid bipedal locomotion which served no doubt as a means of escape. The forelimbs being released could, in moments of need for great speed, become primitive gliding surfaces, by means of which the animal's long strides could be lengthened. This view is supported by the discovery of extinct forms (Ornithischia) which resemble this hypothetical bird ancestor. Such forms may or may not have been close to the line of descent of the birds. It is not impossible that flight was achieved independently by several different reptilian forms, and that some approached flight by one means, some by another.

Thomson (25) has compiled a list of preconditions of flight, i.e., characteristics which it is assumed an organism must have possessed before it was capable of even brief sustained flight. To this he adds a list of accessory adaptations supposed to have occurred subsequent to the beginnings of flight. Inasmuch as the exact sequence of development of such characteristics is largely a matter of speculation and since our chief interest is in bird flight as it occurs to-day, we shall here make no effort to discuss the bird's characteristics in the order of their evolutionary origin.

THE POWER : WEIGHT RATIO

The solution of the problem of true flight presupposes the fulfillment of two conditions. First, the value of the following fraction must exceed a certain minimum:

$$\frac{\text{The power which can be developed by the organism}}{\text{The weight of the organism}}$$

Secondly, the organism must be capable of maintaining the quotient above such a minimum for more than a brief length

of time if flight over a distance appreciably greater than a jump and a glide is to be achieved. It is probable that in very few vertebrates besides birds would this quotient be adequate, even supposing that such forms possessed the means of applying their power efficiently. Most of the characteristics which are responsible for the high quotient in birds are classified by Thomson as "preconditions."

Considering first the numerator of our fraction we must mention the powerful musculature of the typical bird. Those muscles involved in flying, and especially the pectoral muscles which depress the wing, are highly developed. In most birds these muscles compose over one-sixth of the total weight and in certain pigeons they equal in weight the remainder of the bird. If to these huge pectoral muscles we add the other flying muscles and the tendons, bones and feathers directly involved in flight it will be seen that the bird is composed mostly of flying machinery. The remainder of the animal might be considered subservient, being largely organs for the guidance of this machinery and for its nourishment. This last function is of course, most essential. Except in those birds which can, on occasion, soar, sustained flight involves continuous muscle exertion, each individual muscle having but brief, rhythmic periods of relaxation. This would be impossible were it not for the efficient circulatory and respiratory apparatus for the conveyance of nourishment to the muscle tissues and the removal of waste products. The blood of birds contains a larger proportion of red corpuscles than that of any other animal. The heart is powerful and in it we find a completely divided ventricle. Furthermore, the arrangement of the blood vessels is such that there is no admixture of pure and impure blood. In no forms below the birds is this goal attained, although it is approached in some of the higher reptiles. Excellent digestion and respiration maintain the purity of the blood. Examination of bird faeces indicates that birds utilize a far higher proportion of the nutritive value of their food than do mammals, for example. The lungs communicate with air-sacs which are not confined to the thoracic region but often penetrate remote parts of the body, entering bones of the skull, wings and sometimes even the legs and toes. It is said (3) that a bird with a broken wing can breathe through the splintered end of this hollow bone when its windpipe is completely choked with blood. While the air-sacs are important chiefly in connection with temperature regulation it is claimed that they also facilitate respiration. There may be little interchange of gases in them but they assist in the ventilation of the lungs, creating what has been termed a "double-tide" of respiration. Equally important is the relationship of the flying movements to the respiratory movements. The lungs are inexpansible; when relaxed they are filled. The active part of respiration is exhalation caused by compression of the ribs and breastbone, which surround the lungs. The wing movements involve such compression. Thus the more rapidly the wings are moved, the greater the amount of air forced in and out of the lungs. It can be seen that the bird is far less likely to get out of breath than is a mammal, which must accomplish locomotion and respiration by two sets of mechanisms operating separately though of necessity simultaneously. Finally, the bird's capacity for maintaining a constant body temperature results in an efficient operation of the metabolic processes unaffected by fluctuation in environmental tempera-

ture. All these factors and others result in a high rate of metabolism and in the production of great and sustained power.

That the denominator of the fraction, weight, is kept low has already been suggested in our emphasis upon the relatively slight weight of those portions of the animal not immediately involved in locomotion. Surplus weight of all sorts is reduced to a minimum. The body is lean and spare. The reproductive organs are simple and compact and are usually much reduced except during the mating season. The skeletal structure is light, yet strong, largely as a result of fusion of parts. Many individual bones are large, so furnishing ample surface for the adhesions of muscles and tendons and yet they are light, being constructed on the hollow-girder principle. The cross-section of many such bones gives a splendid illustration of economy of material without sacrifice of rigidity. A purposivist should find much pleasure in noting that each bone seems so constructed as to withstand exactly those stresses and strains to which, because of its position and connections, it is subjected.

THE APPLICATION OF POWER TO FLIGHT

But an adequate ratio of power to weight is useless unless that power can be efficiently applied. Obviously, the less efficiently it is applied, the more favorable must be the "power: weight" ratio if flight is to be attained. Probably the most important single item developed by birds in this connection is feathers. True, flight has been achieved by bats without these structures. Nevertheless, feathers, because of their light weight, their impermeability to air, their curvature and general shape, seem to be the ideal material for the construction of planes. Furthermore, a wing which is composed of a number of units, themselves curved and pliable, may, by alteration of the position of these units, be moulded into varying degrees of both curvature and extension to meet the requirements of shifting air currents. The bird-wing, being strong, light, and capable of almost instantaneous alteration of angle and curvature, is likely to prove superior to any planing surface that man will create. Given two such wings and powerful pectoral muscles for their depression there still must be bases for the anchorage of the muscles and a fulcrum against which the wings can pivot. The keel which is developed from the breastbone fills the former requirement. It is lacking or small only in birds such as the ostrich which no longer use their wings for flying. Its development is retained in those birds which have taken to water and use their wings vigorously in swimming. A rigid fulcrum for the wings is supplied by the fusion of the thoracic vertebrae in all flying birds. We thus have outlined briefly the mechanism whereby the wings are suddenly depressed. This is the fundamental movement in the maintenance of the bird in the air. Obviously the wings must be raised between strokes. This is accomplished by the pectoralis minor, a muscle lying ventral to the breastbone. Its *downward* pull is converted into an *upward* pull upon the wings by means of a tendon extending through an opening at the shoulder joint (which thus functions as a pulley) and out to the upper surface of the wing. Besides the structures mentioned there are, of course, many others concerned in the control of the body during flight. Most of these consist of muscles for the alteration of the tail and head positions and for the alteration in flection and curvature of the wings.

Further conditions facilitating the efficient application of the bird's power in flight relate to the general shape and

weight distribution of the body. The bird's body is streamlined, as are those of other forms accustomed to float in a fluid medium. The feather covering adds to this effect by filling in the unevennesses of the surface. Prominent irregularities of surface, as, for example, those formed by external ears, are lacking. As compared with its probable reptile-like ancestors, the bird's tail is shortened and its neck lengthened. The effect is to shift the center of balance further forward. The advantage of this is obvious when it is noted that the supporting wings are attached to the anterior portion of the body. A further condition which tends to stabilize the position of the bird when floating on its wings is the ventral location of the heavier organs of digestion and the dorsal position of the lighter organs of respiration. Finally, since the wings are attached to the dorsal portion of the body, it can be seen that, even though a bird were not to make adequate compensatory movements, it would be indeed a capricious wind which could upset it in the air.

SPECIALIZATIONS IN FLIGHT

While the above remarks are applicable to flying birds in general one must not forget that there are wide variations in the structure and in the flight of birds (Figure 1). Only examples of such can be given here. There is great variation in size of the wings. The smaller the bird the larger must be its wing in proportion to its body size. This is because there is a relatively larger proportion of border area in a small wing and this area possesses less lifting value since the air readily slips past it. The lifting value of various points on the wing surface increases with increase in distance from the edge of the wing. Nevertheless, even amongst birds of the same size we find striking difference in the size, and particularly in the length of the wings. This is usually related to the habitat of the bird. Those living in thicket and forest, like the wren and the pheasant, possess shorter and broader wings, while birds of the open spaces, like gulls and swallows, have long ones. The type of flight depends to a considerable degree upon the amount of effective wing surface. A bird with an abundance of wing surface can afford to flap its wings and glide alternately. Speed is maintained during the glide through loss in altitude. Such a bird can quickly and easily regain the lost altitude. Most of our song birds fly in this fashion. Birds with a smaller wing area in proportion to weight can gain altitude only with difficulty. Having gained it, they prefer to flap their wings continuously rather than to lose it. The grouse and the ducks are examples. The frequency of the wing beat also is related to wing size. Here again there is wide variation, as may be exemplified by the hummingbird at one extreme and the crow at the other. The noise accompanying flight varies from the whistle of the stiff quills of the grouse to the unheard whisper of the downy feathers of the owl.

It can readily be seen that birds cannot be ranked according to their flying ability without taking into consideration the conditions under which flying occurs. No single flying equipment best suits all conditions of wind and calm, of sea and forest, etc. The ability to fly at a great speed or for long distances, to make quick getaways and to dodge and turn with agility, to maintain a constant altitude with a minimum of progression, to dive from heights, these and many other abilities that could be mentioned are so conflicting in their structural requirements that only a few of them are to be found well developed in any one bird. Probably the most striking examples of specializa-

1. Peregrine Falcon.
2. Kestrel.
3. Merlin.
4. Golden Eagle.
5. Montagu's Harrier.
6. Goshawk.
7. Osprey.
8. Sparrow Hawk.

Fig. 1. A Suggestion of the Great Variety of Flight Is Gained by Noting the Variation in Shape and Relative Size of Wings (After Pycraft)

tion for one type of flying condition at the expense of the capacity to meet other conditions is to be found among the soaring birds. Peerless though they are when in "soarable" air currents, they are helpless under many conditions which would hold no terrors for a more generalized bird. The albatross with slim wings and a wing-span of eleven feet is admirably adapted for soaring on the currents deflected upward by waves. But on those rare occasions when the sea is perfectly calm and there is no wind they cannot rise from the water. Vultures, eagles and other large soaring birds have difficulty in rising in a calm unless they can jump from a branch or other high place and so gain the needed momentum by a loss of altitude. They can rise from the level ground only with difficulty and after an awkward run and leap. It is said that they can be trapped by being enticed into a small yard.

GLIDING

We turn now to the modes of flight. It has been said that they are three in number, gliding, flapping and soaring. Although we shall try to show that there is a fundamental similarity between the first and last of these, we shall, for the sake of clarity, take them up in the order just given.

When any body is dropped its fall is impeded by the resistance of the air through which it passes. This resistance increases (approximately) as the square of its speed. If this body is so shaped that in falling it presents a considerable horizontal surface (for example, a sheet of paper dropped flat) the resistance offered by the air is greatly increased. If this object, which is now really a plane, is dropped with the large surface area not lying exactly in the horizontal plane, but tipped, the resultant resolution of forces causes it to make lateral progress during the fall. This progress is in the direction of the lower edge of the plane. Providing our plane is so weighted and shaped that it will maintain the same angle with the horizontal throughout the fall it will continue this lateral progression from the time of its release until it lands. The paper gliders cut out by children neatly illustrate this. All flying birds are capable of this form of gliding. Their curved wings function more efficiently than would straight surfaces. They can maintain and even increase lateral speed at the cost of altitude. By altering the angle of the plane, gliding flight is possible without loss of altitude and even with gain of altitude, but at the cost of lateral speed. When this speed is reduced to nil the lifting effect of the plane is entirely lost. These statements refer to flight in a dead calm or in a uniformly moving body of air. The important points are (1) that gliding requires no other wing movement than adjustment to a suitable angle; (2) that gliding involves either loss in altitude, loss in speed or both. It is obvious, then, that prior to gliding a bird must in some way have gained either altitude or speed. Furthermore, the duration of a glide is definitely limited by the altitude or speed gained.

FLAPPING

The second mode of flight is less limited since in this case it is maintained not at the expense of altitude or speed but at the expense of the energy of the bird. The mechanism for wing movement has been discussed above. The strokes of the two wings occur simultaneously. Were they to alternate, as do the legs of a biped in walking, the bird would roll. Although synchronous action avoids this, it results in an undulating flight. However rapid the strokes and however great the momentum of the bird, there is bound to be a

slight loss in altitude on the up-stroke which is quickly compensated for by a gain on the strong down-stroke. In the case of heavy birds the wing movements of which are slow, this rise and fall can easily be observed. The impulse forward results from the angle of the wings, the down pressure being exerted at the forward edges. This mode of locomotion has been compared to the rowing of a boat. It should be observed, however, that the action of the oars serves to send the boat forward but not to keep it afloat. The bird depends upon its wings for maintenance of altitude as well as for progress. Headley's description of flying (8) is far better. He says that flying consists of a series of jumps in which the bird uses as the fulcrum for each jump, a column of air. The more support the wing finds in a column of air the longer the "jump" that can be made from it. An important point is that the greater the speed of the bird, the greater the air pressure under the wing, i.e., the greater the support in the air column. Speed is, therefore, as important to flappers as it is to gliders. The less the speed the more vigorous must the strokes be if they are to have the same effect. It can readily be seen, then, that the most difficult part of flight is the start. If a bird is on the ground and cannot attain speed by dropping a short distance before rising it must leap into the air, perhaps after a run, and flap its wings violently for several strokes to gain such momentum that less vigorous strokes may be effectual. If a pigeon is observed in his take-off, one can see and hear his wing tips strike each other at the top of each stroke, an indication that his strokes are not merely vigorous but as extensive as possible. It has been observed that if a bird in an enclosure is frightened off the ground several times in quick succession it begins to breathe hard, and eventually refuses to take wing. Headley emphasizes the fact that birds appear to prefer to fly in air that has not just been ruffled by another bird. In migration formations each successive bird follows not exactly in the wake of its predecessor but to one side. Presumably,

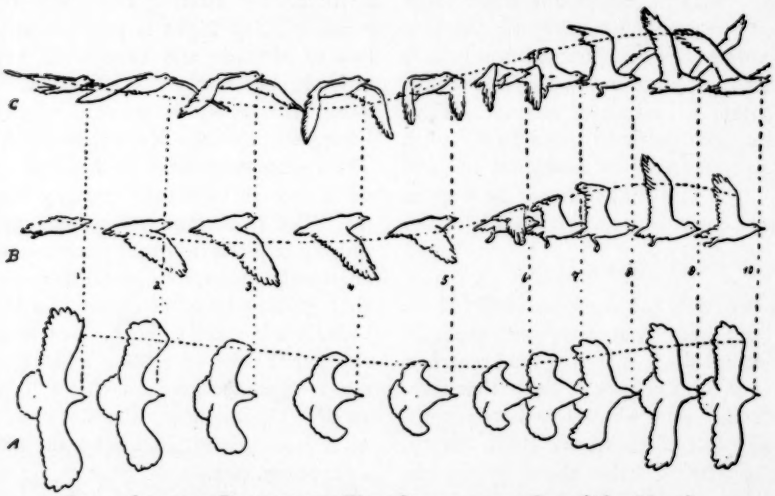

FIG. 2. SUCCESSIVE PHASES OF THE WING STROKE IN THE GULL (After Marey)

this is so in order that, for each stroke, the bird will be supplied with a fresh, undisturbed column of air. The hovering in

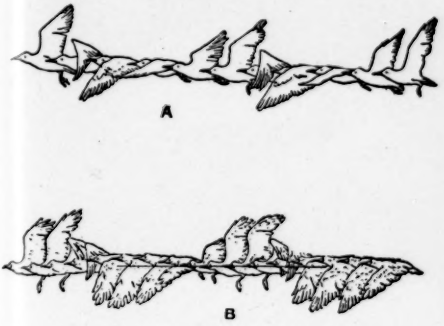

FIG. 3. SUCCESSIVE PHASES OF THE WING STROKE IN THE GULL

A. Twenty-five photographs per second. B. Fifty per second. (After Marey.)

one place which is accomplished by humming-birds, appears to be an example of flight in which a fresh column of air is not supplied for each stroke of the wings. It has been claimed, however, that such

FIG. 4. THE START, A PHOTOGRAPH TAKEN JUST AFTER THE LEAP

Note position of tail and contrast with Figure 5. (After Headley.)

hovering occurs only when there is sufficient wind to supply each stroke with a new column. In any case, only the very strongest flyers are capable of hovering.

Motion picture photography has opened the way to analysis of the strokes of the wings. The chief fact revealed is that in

FIG. 5. PIGEON ALIGHTING

Note braking by wings and tail, and preparation of feet. (After Headley.)

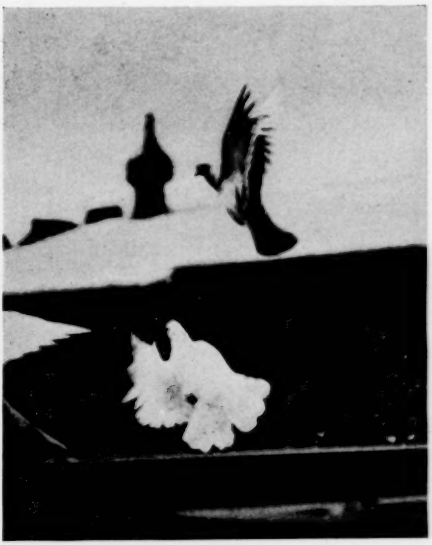

FIG. 6. PHASES OF THE WINGSTROKE

1) At the top of the upstroke, ready for the down-stroke. (After Headley.)

the up-stroke the wing does not simply reverse the motion of the down-stroke. The angle of the wing is slightly altered

and the pressure with which adjacent feathers had been held together on the down-stroke to prevent leakage, is relaxed. Furthermore the wings do not execute a simple rising-falling movement but also a fore-and-aft motion. If the motion of the wing tips were graphed against a surface moving with the speed of the bird they would register a sloping figure 8 (Figure 10).

The curvature of birds' wings is apparently calculated to produce the maximum resistance to the down-thrust and at the same time to offer the minimum resistance to the forward movement of the bird. Comparative studies show that, in general, the wing curvature is greater

FIG. 8. PHASES OF THE WINGSTROKE
3) During the upstroke the feathers are spread. (After Headley.)

FIG. 7. PHASES OF THE WINGSTROKE
2) The feathers make airtight contact during the downstroke. (After Headley.)

in the heavy, slow fliers (where the lift is of greatest importance) than in the rapid fliers. Similarly, the slow-moving portion of the wing near the body of the bird is deeply curved whereas the rapidly moving tip is flattened. The bird has been justified by physical formulae in this matter and, as a result, the wings of high-speed aeroplanes are built almost flat and those of slower machines designed to carry great weights are more deeply curved.

Control of the direction of flight, both vertical and horizontal, might conceivably be accomplished by the wings. It is probable that horizontal control, steering to the right or left, is chiefly accomplished through their efforts, but not, as in rowing, by a more vigorous backward thrust of one wing or the other. Rather, there is a stronger downward thrust of one wing which results in a partial rotation of the bird on its anterior-posterior axis. This "banking" accompanied probably by slight tail elevation, results in a turn toward the side of the depressed wing. The tail probably acts not as the rudder of an aeroplane, but as do the elevating planes. The latter are effective in turns in the horizontal plane when an aeroplane is steeply banked. Control in the vertical plane, especially as this is necessary in landing, is effected, at least partly, through tail action. Observation of the alighting of a large bird clearly demonstrates the cooperation of wings and tail in the process of vertical control and also in "braking" or overcoming the momentum of flight.

There are wide differences among birds

in the ability to control flight and especially in the facility with which they can shift the horizontal or vertical direction

FIG. 9. PHASES OF THE WINGSTROKE
4) A late stage in the upstroke. (After Headley)

of their course. Many small birds can dart to right or left, up or down, with such suddenness as to escape from hostile birds capable of more rapid flight but not of sudden change in direction. The duck is an outstanding example of a bird capable of acquiring terrific momentum in a straight line but not of quick shift in direction.

SOARING

While flapping is the most usual form of flight, this very fact makes it less interesting than soaring. Furthermore, the theories with which writers have cloaked the apparent mystery of soaring flight add to the interest of the subject. The following are among the better known soaring birds: eagles, falcons, buzzards, pelicans, vultures, adjutant storks and albatrosses. Examination of such birds shows that they possess a high ratio of sail area to total weight. A high ratio of power to weight is found in all birds, of course, but this is not so important for soaring birds as is a high ratio and proper arrangement of sail area, or lifting surface. Because of the fact that soaring depends upon the lifting value of the practically motionless wings it is important that the arrangement of lifting surface be such as to yield the maximum value. In two ways, especially, is this effected. Since the front half of any plane possesses higher lifting value than the rear half, the wings of soarers are generally much longer and narrower than those of non-soaring birds. Such extreme length would prove unwieldly for a bird which flapped its wings. In the second place, the curvature is such that all parts of the wing surface, even the rear portion, are as effective as possible. As noted above, the degree of the most efficient curvature varies with the speed with which the wing passes through the air. Since in soaring this rate is subject to constant alteration (in fact, we shall see that soaring depends

FIG. 10. PHOTOGRAPHIC TRAJECTORY OF THE TIP OF A CROW'S WING WHILE IN FLIGHT
Arrows show direction of the tip's movement, which is such that the bird is driven forward by the down stroke. (After Marey.)

upon this alteration) it is essential that the wing curvature be subject to continual modification to suit these changing conditions. Unless a method for such change of curvature can be devised in man-made gliders it seems inevitable that they should remain far inferior to soaring birds. The construction of the wings of gliders so

that a portion is hinged and movable approaches the solution of this problem. Warping of the wings would be preferable, however.

A description of soaring should begin with discussion of the air conditions necessary. Soaring appears never to have been observed in a dead calm. It usually occurs when there is a good breeze. It is frequently seen over rolling country and over waves. A choice spot for soaring seems to be above a sea cliff. Soaring occurs most frequently in semi-tropical countries which are subject to extreme variation in temperature. In such countries it may occur in the middle of the day even when there is only a slight breeze and even over level country. It may occur at almost any altitude, although the range is limited by conditions to be noted below.

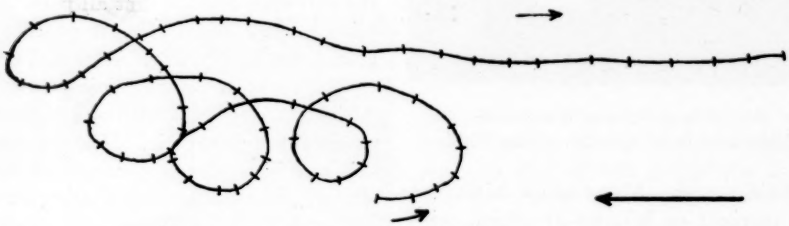

FIG. 11. ONE OF HANKIN'S MIRROR TRACINGS OF A SOARING BIRD
The track is marked at one-second intervals. (After Hankin)

While soaring, a bird's wings are not held rigid, but are subject to constant slight alteration in angle and in flection. There are movements of the wings at the shoulder and elbow and of the tail feathers, neck and head. The bird's speed and direction are constantly changing. There is continual shifting of the right-left and fore-aft angle at which it is tilted. Its altitude, too, constantly fluctuates. The rhythm of rise and fall is usually not periodic while that of turning in the horizontal plane is more often so.

In the most usual form of soaring, the bird circles slowly. There is, however, considerable difference from one species to another with respect to soaring movements and the only generalization that can legitimately be made is that a soaring bird is never seen to maintain any given direction or speed for more than a moment at a time. While there are many pages devoted to the description of soaring birds few of them are as adequate as those of Hankin (7). His observations were made upon only a few species, chiefly vultures, kites and marabous, but they are of special value because they extended over a considerable period of time. The accurate observation of the flight of birds at great heights requires training that comes only with such long study. In addition to direct observation of the birds by eye and binoculars, Hankin employed a mirror device which permitted him to make accurate tracings of the course of a bird (Figure 11). Furthermore, a time marker was used so that later calculations could be made of the speed of the bird (in the horizontal plane) at any part of its course. Hankin wastes few words on theory, being satisfied to present as full a description of the facts as possible. It is regrettable that others have not extended his work to the many other soaring birds. A few of the important observations he has made will

be noted in a later paragraph, but the reader must be referred to the original for details.

Many of the theories of soaring which have been contributed are entirely inadequate. By no means all of them will be considered here. There is a theory which deserves attention only because its acceptance has caused some confusion. It is based upon the false assumption that just as a kite can rise in a strong wind, so can a bird. In the following discussion it should be clear that we are referring to a wind moving in the horizontal plane only, moving at a constant speed, and as a unit. A moment's consideration will indicate that a bird flying in such a body of air has no advantage over one flying in a perfect calm. In fact, a bird could not detect which of these two conditions held except by some reference (probably visual) to the earth beneath. The movement of the wind has in itself no lifting value except to an object which possesses and can maintain inertia antagonistic to such movement. A kite can stay up only so long as its string is intact. When this is cut it must fall (and would even if so balanced as to maintain an appropriate angle) for the difference in inertia it recently possessed is quickly overcome.

This theory has been applied by Ahlborn (according to Prochnow (21)), especially to birds which circle. Ahlborn maintains that when they move with the wind they acquire velocity with perhaps a slight loss in altitude, and that when they then wheel into the wind this velocity is converted into altitude. Certain of Hankin's observations appear to lend support to this view since they indicate that the speed of the bird is least on the windward side of the circle, followed by a sudden increase in speed as the bird goes down wind. The theorizers do not seem to have considered the fact that the gain in altitude when the bird turns into the wind is made only at the cost of speed and with the result that, with each succeeding circle, there must be loss of distance to the leeward. Hankin and others have observed a bird circle for hours without such loss. If a bird could maintain altitude (without effort on its own part) by merely circling in a uniform wind it could maintain altitude by circling in a dead calm. This would be equivalent to perpetual motion.

Exner (5) (6) suggests that what appears to be soaring flight is really a modification of flapping flight. He supposes the wings to be moved with great rapidity and within very narrow limits. He offers little proof but calls attention to the rapid wing movements of insects and suggests that a somewhat similar humming sound can be heard emanating from soaring birds. The theory seems to have been adequately refuted (21) (24).

Besides these theories which appear to be quite inadequate there are three which are more acceptable. Each emphasizes a factor which doubtless operates in certain instances. We do not claim that any one of these factors alone or all taken together adequately accounts for all soaring although this may be the case. The present need is for more extensive and detailed records of soaring flight and of air conditions during such flight.

1. The theory of the direct variation of air velocity with altitude

To understand the merits of this theory one must bear in mind the conditions under which wind can be utilized by a bird to gain altitude. Wind in itself cannot be converted into lift except by a plane possessing inertia which is to some degree antagonistic to that of the wind. When a bird leaps from the ground against the wind it possesses this inertia, and the

wind striking the under surface of the wing is a lifting as well as a retarding force. If the wind be constant in speed at all levels its retarding influence will soon result in the loss of the bird's original inertia. The animal then will be borne along with the wind and all lifting force will cease. If, however, we were to assume that with each slight gain in altitude the bird encounters air which is moving more rapidly than that which it has just left we can see that the bird would always possess inertia to some degree antagonistic to each succeeding level of air. This assumption may be justified for wind currents near the earth's surface because the friction of the earth must be considerable. Headley (8) has demonstrated this difference in speed at different levels, using an anemometer. On one occasion he recorded a velocity of 770 feet per minute at a height of two feet from the ground when the velocity was 1000 feet at a height of seven and a half feet. Idrac's observations of the albatross (9) (10) indicate that the soaring of this bird is largely dependent upon velocity inequalities in the air immediately above the waves. The albatross constantly rises and falls above the water but it never attains any great altitude.

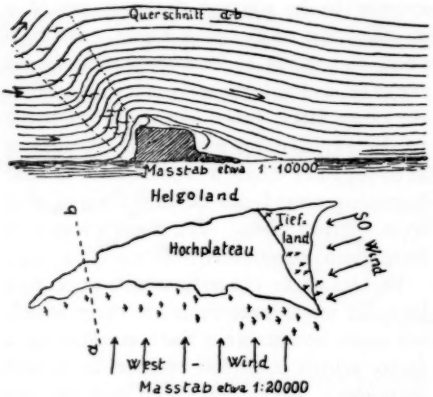

FIG. 12. DRAWING TO DEMONSTRATE RISING CURRENTS, CAPABLE OF SUPPORTING A SOARING BIRD, WHICH RESULT FROM DEFLECTION OF THE WIND BY A CLIFF OR HILLSIDE

(From Nimführ, R. 1919. Mechanische und technische Grundlagen des Segelfluges. Berlin. R. C. Schmidt.)

Many birds soar at heights of a thousand feet and more. It is improbable that at these heights the retarding influence of the earth upon the wind should result in sufficient velocity differences to account for soaring. This theory seems applicable only to flight within a few score feet of the earth's surface.

2. The theory of upward currents of air

The "bumps" encountered by aeroplanes furnish familiar evidence that there are air currents in other than the horizontal plane. There are three chief sources of such: the deflection of wind by irregularities in the earth's surface, the temperature changes resulting in rising and falling columns of air, and the deflection upwards of one air current by another.

Under certain conditions the upward movement of the wind is so pronounced that birds which cannot (or do not) ordinarily soar have been observed to perform maneuvers which might be described as such. Cliffs, hills, buildings, waves and ships may serve as deflectors (Figure 12). Birds which skim ocean waves no doubt are aided by such currents. Hankin notes that birds could soar over a tall fortress if there were a breeze, even when the air was otherwise (as will be noted below) unsoarable.

The significant relationship between temperature changes and the soaring of certain birds is emphasized by some of Hankin's observations. He classified birds with respect to their ability to

soar (on the basis of their speed in gaining altitude, their structure, etc.) and observed that under some conditions no birds would soar, at other times only the best soarers would rise while under the most favorable conditions even the poorest were successful. Early in the morning none would rise. First the best soarers appeared and only later the heavier and less able birds. The birds ceased soaring in the late afternoon in the reverse order. It seems evident that with the heating of the earth by the sun, and thus of the air nearest the earth, a constant upward current was produced. Under the most favorable temperature conditions soaring was possible even though the wind velocity was very slight. At other times soaring required a good breeze.

In the third source of upward currents of air mentioned above, the deflection of one air current by another, we have a factor which is operative whenever there are appreciable air movements. When two gusts meet each other head on or at an angle there results deflection both upward and downward. The vertical movement is not so steady as that resulting from temperature changes or deflection by cliffs. Nevertheless, such thrusts may be strong while they last. The problem of the bird is to utilize all such vertical movements. The upward thrusts are capitalized to the fullest by appropriate wing expansion. The effect of the downward thrusts is minimized by alteration of the angle of the wings. The curvature of the wing surfaces is such as to aid in this process. The convex upper surface offers the minimum resistance to down-currents. The pressure on this surface is kept low since the air readily slips off the edges of the wing. The concave lower surface, on the contrary, cups the wind and wastes little of the available upward pressure.

3. A new theory

The first two theories assist in the understanding of many instances of soaring. Nevertheless, there appear to be cases for which they alone cannot adequately account. How can a bird maintain its altitude in the absence of vertical air-currents (theory 2) and at heights too great for theory 1 to operate?

Insufficient attention has been given to the fact that most wind is gusty. Even a "steady" breeze is subject to constant fluctuation in speed and direction. In assuming such fluctuation it seems that we are not going beyond the facts. Given such fluctuation we are possessed with the basis of antagonistic inertia, that material which a soaring bird so efficiently converts into altitude. Let us assume that the bird is gliding into a wind. This air current suddenly eases and at the same time a current from a slightly different direction strikes its wings. The bird now possesses inertia antagonistic to this new gust and by wheeling can at once capitalize the difference in direction to the advantage of its altitude. The process continues indefinitely as the bird continually meets with irregularities in the air. Each such irregularity is the source of a stress which, theoretically, is capable of conversion into lift. Thus, there is constant readjustment to constantly shifting currents. Quite naturally a bird must, in the course of this procedure, adopt a circular or elliptical course if it is to remain soaring above a single section of the countryside, as any other course (excepting a much more involved course, such as a figure 8) would carry it away from its chosen position. Perhaps the greatest mystery of soaring is that which is usually taken for granted, the great sensitivity of the bird to shifting air-currents and the remarkable ability for rapid, coordinated and appropriate responses to these stimuli.

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NEW BIOLOGICAL BOOKS

The aim of this department is to give the reader brief indications of the character, the content, and the value of new books in the various fields of biology. In addition there will frequently appear one longer critical review of a book of special significance. Authors and publishers of biological books should bear in mind that THE QUARTERLY REVIEW OF BIOLOGY *can notice in this department only such books as come to the office of the editor. The absence of a book, therefore, from the following and subsequent lists only means that we have not received it. All material for notice in this department should be addressed to Dr. Raymond Pearl, Editor of* THE QUARTERLY REVIEW OF BIOLOGY, *1901 East Madison Street, Baltimore, Maryland, U. S. A.*

BRIEF NOTICES

EVOLUTION

THE NEW EVOLUTION. ZOÖGENESIS.
By Austin H. Clark.
The Williams and Wilkins Co.
$3.00 $5\frac{5}{8}$ x $8\frac{1}{2}$; xiv + 297 *Baltimore*

In this book Dr. Clark presents a graphic picture of the plasticity of the organism and the closeness and complexity of its relation with the environment. No recent work on evolution has stirred up such impassioned controversy as has this book. It has, indeed, risen to the heights of calling Dr. Clark bad names. The gist of his evolutionary doctrine is summed up in the following passage:

In tracing the history of animal life from its very first appearance to the infinite complexity which we see at the present day there are three entirely separate sets of facts to be considered, and any acceptable theory of the development of animal life must harmonize and correlate all three.

In the first place, within each of the so-called phyla or major groups of animals, as is well seen in the vertebrates, particularly in the mammals and the reptiles, there are many well marked, obvious, and undeniable evolutionary lines which, beginning with a relatively simple form of creature run by easy stages to a specialized and highly complex form.

In the second place, very few of these evolutionary lines are perfectly continuous. Practically all of them are more or less interrupted by gaps of various widths, and these gaps are often very broad. Especially is it true that these evolutionary lines tend to be separated from each other for their entire course, running parallel or more or less convergent right down to their very earliest beginnings, and not uniting in a common type of animal as we would expect. For instance, the whales and the seals are always whales and seals, and show little or no approach to any other type of mammal. Similarly, there are no intermediates between turtles and snakes, or between turtles and lizards, all of which are reptiles, or between squid and oysters, though both types are mollusks.

In the third place, no animals are known even from the very earliest rocks which cannot be at once assigned to their proper phylum or major group on the basis of the definition of that group as drawn up from a study of living animals alone. A backboned animal is always unmistakably a backboned animal, a starfish is always a starfish, and an insect is always an insect no matter whether we find it as a fossil or catch it alive at the present day. There can be only one interpretation of this entire lack of any intermediates between the major groups of animals, as for instance between the vertebrates, the echinoderms, the mollusks and the arthropods. If we are willing to accept the facts at their face value, which would seem to be the only thing to do, we must believe that there never were such intermediates, or in other words that these major groups from the very first bore the same relation to each other that they do at the present day. Is this creationism? Not at all. It simply means that life at its very first beginnings from the single cell developed simultaneously and at once in every possible direction. All of the phyla

or major groups seem to be of simultaneous development—at least we have no evidence that it was otherwise. From each one of these a separate developmental line or tree arose, growing upward through the ages.

THE PROGRESS OF LIFE. *A Study in Psychogenetic Evolution.*
By Alexander Meek.
Longmans, Green and Co.
$4.20 5½ x 8½; vii + 193 *New York*

The opening sentences of the preface of this book read:

> This work is not meant to introduce a new theory but to indicate a way to recover that elasticity of conception of the processes of evolution which the behaviour of protoplasm invites and which the germplasm theory of development has for so many years prevented. The inadequacy of the theory has become more and more apparent and in my opinion the time for its recession has been long overdue.

So far as we have been able to determine, the author has stated little that is new, and a good deal that seems questionable. Exactly what his position is we have not discovered; he appears, however, to be a follower of Butler and Semon. He emphasizes at length the fact that the environment plays an important part in determining the characteristics of the individual. The briefest statement of his views is given at the end of Chapter V:

> The free cell and the germ cell, each of them, can do nothing else but give rise by growth to the kind of cell or the kind of soma from which it has arisen, and it needs to accomplish the history an environment which supplies the food and the energy.

We cannot avoid the suspicion that the somewhat confused language in which the book is written may derive in some measure from a lack of clarity in the ideas of the writer.

THE GENETICAL THEORY OF NATURAL SELECTION.
By R. A. Fisher. *Oxford University Press*
$6.00 6¼ x 9¼; xiv + 272 *New York*

This book falls into two sharply contrasted parts, in the first of which Dr. Fisher speaks with the accent of the physical biologist, but in the second with that of the eugenist. The direction of evolution, he concludes, is determined, not by the direction of mutation but by that of selection. To the reviewer this conclusion seems in some part paradoxical. Can any selective process, however stringent, succeed in drawing a population of green balls from an urn containing only black balls? And, if some of the black balls mutate to red, does the resulting increase in variance in any way aid selection in its task of picking out the green balls that are not there? Of course, if black balls mutate to both red and green but more frequently to red, selection may pick out the rare green mutations rather than the more common red ones, but in this case both mutation and selection have their effect on the direction of evolution.

THE KEY TO EVOLUTION. *In Four Double Volumes. Vol. 1, How Life Began. Vol. 2, How Plants Arose. Vol. 3, The Origin of Animals. Vol. 4, The Origin of the Backboned Animals. Vol. 5, From Amphibian to Man. Vol. 6, Man, Cousin to the Apes. Vol. 7, Embryology and Evolution. Vol. 8, Causes and Methods of Evolution.*
By Maynard Shipley. *Haldeman-Julius Co.*
Girard, Kansas
$2.45 for set of four double volumes
5½ x 8⅓; 64 pages each (paper)

Why is Haldeman-Julius permitted to stay in business in Kansas? This problem has long troubled us. Have the Ku Kluxers no pride, that they have not tarred and feathered him long since? Anyhow, they have not, and he continues

to publish incendiary and blasphemous stuff, and, presumably, to sell it in quantity. The present work is an unusually ambitious one. It attempts to tell the whole story of evolution, from the Galaxy to *Homo sapiens*, with full documentation, and frequent beltings of the Fundamentalists and Henry Fairfield Osborn. It is, incidentally, quite well done.

STUDIES ON THE EVOLUTION OF THE PELVIS OF MAN AND OTHER PRIMATES. *Bulletin of The American Museum of Natural History, Vol. LVIII, Art. XII.*

By Harriet C. Waterman.

American Museum of Natural History

65 cents $6\frac{1}{4}$ x $9\frac{1}{2}$; 58 (paper) *New York*

The author bases her study upon the form of the pelvis of man and other primates and the function of the muscles involved. In the summary there is given a list of the "habitus and heritage characters in the ilium and ischium of the animals studied," also a list of "the habitus and heritage characters in the musculature of the main groups." Her conclusions support Gregory's (1920) views as to the main stages in the evolution of the pelvis from the primitive arboreal quadrupeds to man. The report includes tables of measurements of bones and muscle fibers of the forms under consideration and figures of pelvic and femoral bones and their musculature. There is a bibliography of 32 titles.

GENETICS

EINFÜHRUNG IN DIE VERERBUNGSLEHRE.

By Erwin Baur. *Gebrüder Borntraeger*

21.50 marks $6\frac{5}{8}$ x 10; vii + 478 *Berlin*

A revision of this excellent introduction to the study of inheritance which is by way of becoming a classic textbook. Rather more attention is given to the botanical side than most texts allot, and there is perhaps less tendency to assume that *Drosophila* suffices to explain all heredity in every organism. The book is profusely illustrated, has a good index, and an excellent list of literature for the student.

GENETICS. *An Introduction to the Study of Heredity.*

By Herbert E. Walter. *The Macmillan Co.*

$2.50 $4\frac{7}{8}$ x $7\frac{1}{4}$; xxi + 359 *New York*

The author has completely overhauled this book, and brought it well up to date. It is a thoroughly sound textbook written in the author's usual delightful style. No college student of zoology should fail to read it.

DAS DETERMINATIONSPROBLEM IN ANALYTISCHER DARSTELLUNG.

By Adolf Cohen-Kysper. *Julius Springer*

4.80 marks $6\frac{1}{2}$ x $9\frac{1}{2}$; 48 (paper) *Berlin*

A discussion of the factors underlying ontogenesis, which emphasizes that the genes are not independent factors, each producing its effect on development in isolation from the others, but that the organism as a whole is a system, the parts of which are in their turn systems of lower order, and so on. The author warns that the results obtained in experiments on regulation may lead to misinterpretations when applied to questions of normal development.

LES GROUPES SANGUINS. *Schémas et Applications Pratiques.* LA TRANSFUSION SANGUINE. *Technique et Indications.*

By Paul Michon. *Masson et Cie*

16 francs $5\frac{1}{2}$ x $7\frac{7}{8}$; 120 (paper) *Paris*

A brief account of blood-groups, and of the technique of blood transfusion.

MENDEL'S PRINCIPLES OF HEREDITY, *Fourth Impression.*
By W. Bateson. *The Macmillan Co.*
$5.00 6 x 9; xiv + 413 *New York*

GENERAL BIOLOGY

THE USE OF THE MICROSCOPE. *A Handbook for Routine and Research Work. By John Belling. McGraw-Hill Book Co., Inc.*
$4.00 $5\frac{3}{4}$ x 9; xi + 315 *New York*

This book contains much valuable information, badly presented, for the practising worker with the microscope who has a reasonable familiarity with the theory of his instrument. It is not a book that will be of much service to the beginner. To take one example: We find on page 19 the statement "There can be no understanding of the microscope without understanding aperture;" but we defy anyone to arrive at an understanding of aperture on the basis of what is to be found in this book. There is an index, not too good, and a bibliography of 157 titles.

ÜBER DEN UNTERSCHIED VON MINERALIEN UND LEBEWESEN. *Öffentlicher Vortrag, gehalten am 18. Dezember 1929 in Berlin.*
By Arrien Johnsen.
Gebrüder Borntraeger
4.50 marks $5\frac{1}{2}$ x $8\frac{1}{2}$; 41 (paper) *Berlin*

We have already been instructed by an eminent physicist on "How to Tell the Birds from the Wild Flowers." In this interesting lecture an eminent mineralogist considers some of the likenesses and differences between minerals and living beings. Crystals, like living beings, undergo growth, regeneration, natural selection, and mutation. Heterogeneity is, however, a necessary, though not a sufficient condition of living substance. In this respect amorphous minerals stand nearer to living beings than do crystals.

FIELD BOOK OF PONDS AND STREAMS. *An Introduction to the Life of Fresh Water.*
By Ann H. Morgan. *G. P. Putnam's Sons*
$3.50 $3\frac{3}{4}$ x $6\frac{3}{4}$; xvi + 448 *New York*

Dr. Morgan, Professor of Zoology of Mount Holyoke College, is by her training as a teacher and a collector well fitted for the task which she has set herself. Not only has she produced a thoroughly dependable guide but a fascinating one. The numerous illustrations in color, half-tones and black and white drawings, have been fittingly chosen. The keys make identification of the different species a simple matter. There is a lengthy bibliography, a glossary and an excellent index.

LA SOLUTION DU MYSTÈRE DE LA MORT.
By J. L. W. P. Matla. *Gaston Doin et Cie*
65 francs (paper) *Paris*
75 francs (cloth)
$6\frac{1}{4}$ x $9\frac{1}{2}$; vi + 284 + 6 plates

A description of experiments to determine the volume of the soul, which, the author concludes, is material and therefore not immortal, but continues to exist for a limited time after the death of the body. It is not altogether surprising that his conclusion has failed to commend itself to either physicists, spiritists, or the orthodox religious.

THE SCIENCE OF BIOLOGY. *An Introductory Study. Revised Edition.*
By George G. Scott. Thomas Y. Crowell Co.
$3.75 5⅝ x 8⅜; xx + 633 *New York*

The revised edition of this excellent text retains the plan by which the different plant and animal phyla are studied before considering general biological problems. The book is clearly written and covers a wide range of topics.

BIODYNAMIQUE GÉNÉRALE. *Fondée sur l'Étude du Tourbillon Vital d'Éther.*
By Alfred Lartigue. Gaston Doin et Cie
20 francs *Paris*
5⅝ x 9⅛; iv + 156 (paper)

M. Lartigue wishes to base the structure and functions of living beings on vortices in the ether. The argument suffers from the defect common to arguments from *simulacra vitae:* the likeness of two patterns does not necessarily prove the likeness of the causes producing them.

DICTIONARY OF BIOLOGICAL EQUIVALENTS. *German-English.*
By Ernst Artschwager.
The Williams and Wilkins Co.
$4.50 6 x 9; 239 *Baltimore*

A useful book for the student of biology. The author has succeeded in being a far more complete and thorough lexicographical help to the biologist than have any previous dictionaries. The English meanings for the German words are well chosen.

FOUNDATIONS OF BIOLOGY. *Fourth Edition.*
By Lorande L. Woodruff. The Macmillan Co.
$3.50 5½ x 8½; xvi + 501 *New York*

MANUAL OF BIOLOGY.
By George A. Baitsell. The Macmillan Co.
$2.60 5½ x 8½; xiv + 369 *New York*

New editions of these well known texts, which have been worked out for use together.

EINFÜHRUNG IN DIE BODENKUNDE DER SEEN. *Die Binnengewässer. Band IX. By Einar Naumann.*
E. Schweizerbart'sche Verlagsbuchhandlung
16 marks (paper) *Stuttgart*
17.50 marks (cloth)
6¾ x 10; ix + 126

A TEXT-BOOK OF BIOLOGY. *For Students in General, Medical and Technical Courses; Sixth Edition, Thoroughly Revised.*
By William M. Smallwood. Lea and Febiger
$4.00 net 5¾ x 9⅛; 470 *Philadelphia*

LABORATORY MANUAL OF GENERAL BIOLOGY
By George G. Scott. Thomas Y. Crowell Co
$1.00 5½ x 8⅝; xi + 125 *New York*

LABORATORY STUDIES, DEMONSTRATIONS, AND PROBLEMS IN BIOLOGY.
By Nathan H. Kingsley and Edward J. Menge. Bruce Publishing Co.
$1.28 8½ x 11; 208 (paper) *Milwaukee*

HUMAN BIOLOGY

ROCK PAINTINGS OF SOUTHERN ANDALUSIA. *A Description of a Neolithic and Copper Age Art Group.*
By Abbé Henri Breuil and M. C. Burkitt, with the collaboration of Sir Montagu Pollock.
Oxford University Press
$25.00 *New York*
10 x 12½; xii + 88 + 33 plates and 7 maps

An account, with many excellent plates, of the neolithic and copper age paintings in the rock shelters of southern Spain.

It is an important as well as a very interesting book. The bulk of the work upon which this book is based is due to M. Breuil. Sir Montagu Pollock translated the condensed notes, and contributed a good deal on nomenclature. Mr. Burkitt contributed the Introduction and Conclusion, as well as some of the photographs.

There are generally recognized now three "groups" of prehistoric Spanish art. The first of these art groups is typified by the paleolithic cave paintings, of which the best example is the wonderful frescoed ceiling of Altamira. Some of our readers will perhaps be surprised to learn that Mr. Burkitt, in this book, dates these paintings with the following statement: "The visitor . . . . can only rest amazed at the artistic ability of these early folk who lived perhaps ten thousand years and more ago." We should have thought a good deal more.

Art Group II is the earliest rock shelter art of eastern Spain. This art Burkitt believes to be not far in date from the cave art of Art Group I, though so different from it as to indicate that entirely different tribes of people were involved in its doing. It is characterized in two ways: first, the animals differ from the Group I animals in the same sort of way that the animals of a good Japanese artist differ from those of Rosa Bonheur; second, human figures are frequent, whereas they occur only rarely in cave art.

Art Group III is another, and presumably much later, rock shelter art, which has its center and focus in Andalusia, though much of it is found in the provinces of southern Spain further to the east. It is with this Art Group III that the present book is concerned. It is characterized primarily by its completely conventionalized patterns, or symbols. These paintings are often found superposed upon paleolithic Group II drawings on the same rock walls.

The authors are extremely cautious and conservative in the matter of conclusions. As to dating they make at least a plausible, if not quite conclusive case, that the painters were of a neolithic and perhaps copper age culture. As to the motive and meaning of the paintings no conclusion is reached. Various possibilities (religious, marriage, talismanic protection, etc.) are suggested, but they carry no conviction.

The book must be regarded as a splendid objective record of an extremely interesting lot of artefacts made by prehistoric man. The interpretation of this record must wait upon further research.

CAUSES OF DEATH BY OCCUPATION. *Occupational Mortality Experience of the Metropolitan Life Insurance Company, Industrial Department 1922–1924. Bulletin of the United States Bureau of Labor Statistics No. 507.*

By Louis I. Dublin and Robert J. Vane, Jr.

U. S. Government Printing Office

25 cents *Washington*

$5\frac{3}{4}$ x $9\frac{1}{8}$; iv + 130 (paper)

This study is based upon a group of industrial policy holders (105,467 white males) of the Metropolitan Life Insurance Company, whose occupations were in manufacturing plants, mines, transportation, industries and mechanical plants. The statistics deal with occupied individuals who died during the years 1911–13 and 1922–24. Space will permit only a few of the interesting results which the analysis of this data shows. It is found that

within the same social class the death rates of male wage earners are uniformly higher than those of females. Their death rates also exceed those prevail-

ing among males in the general population and among males insured under ordinary policies in the same company. Differential death rates of various age groups show that this disparity increases year by year up to about age 54. Compared with workers in nonhazardous employments, wage earners are at a disadvantage in respect to every important cause of death. The death rate from tuberculosis, age for age considered, is especially high in the industrial group and ranges from two and a half to nearly four times that of the nonindustrial population. Deaths from pneumonia and accidents are over twice as frequent; while death rates from the degenerative diseases are from two to three times as great.

There are 78 tables in the text and a list of 26 references is given.

HANDS AND FACES. *The Book of Temperaments. Being the Third and Concluding Volume of "The Book of the Hand."*
By Katherine St. Hill. *Rider and Co.*
10 shillings 6 pence net *London*
6 x 9; 160

In this book the author turns from palmistry to physiognomy, illustrating her types with the portraits of historical personages. "I should very much have liked to adorn my pages and portray my characters with examples of living personages of great importance, but I have been advised by the wise and learned that if amid my studies the cap which fitted was not of the most laudatory I should be in danger of actions for libel, and on the axiom that 'the greater the truth the greater the libel' I could be seriously punished."

The book cannot be taken as a serious contribution to the interesting but difficult subject of constitutional types; the author has, however, a sharp pen and such bits as the following will repay the casual reader:

> Venus-Luna is very ineffective and helpless. These subjects always want to be worked for and taken care of. "They want to go to Heaven in a handbasket," as an old Devon woman said of one of them. Whatever they have in the world they cannot hold on to, and are soon robbed of it by some clever Mercurian or greedy Saturnian person. But if properly guarded and cared for they are gentle and grateful, and never rebel against coercion. They love quiet and comfort, and will employ themselves in all sorts of little kind actions, and are often very restful if not very intelligent companions to the more strenuous temperaments. They go into the Church, and are good curates, considerate, pious, and sympathetic. The women take to writing verse and visiting cottages.

GRUNDZÜGE DER VERERBUNGSLEHRE, RASSENHYGIENE UND BEVÖLKERUNGSPOLITIK *für Gebildete aller Berufe.*
By Hermann W. Siemens.
J. F. Lehmanns Verlag
3 marks (paper) *München*
4 marks (cloth) $4\frac{7}{8}$ x $7\frac{1}{2}$; 147

The fourth edition of this popular tract on heredity and eugenics, which has been translated into Swedish, English, and French (a Dutch translation is announced). As this type of uplift goes, the book is well done. Some of the data introduced, however, rather give us pause. For example, we find the following table showing the relation between the price of hats and the sizes available at these prices:

Price of Hat marks	*Largest available size*	*Mean size*
3	56	54
6	57	55
7	59	56
12	60	57
24	61	58

The argument then runs: high-priced hats are larger. Therefore the people who buy them have bigger heads; but brain size is correlated with head size, and mental endowment with brain size; hence the rich are better endowed mentally than the poor.

A HISTORY OF THE JEWS.
By Abram Leon Sachar.
Alfred A. Knopf, Inc.
$5.00 6¼ x 9¼; xli + 408 *New York*

To write a history of the Jews is an ambitious undertaking and to compress it into one volume is indeed a difficult task. One cannot but feel upon laying down this book that the author still has much to say. Nevertheless he has contributed a highly interesting and authentic account covering thirty centuries of Judaism. Throughout the book, whether in discussing the golden age of the Jews in Moslem Spain, the ghetto, Jewish mysticism, the influence of the French Revolution upon the Jews, the Russian pogroms, or the Jew in the new industrial world, the author has maintained a singularly objective viewpoint. Of especial interest to readers of these pages will be the sections dealing with the history of the Jews in America. The work includes eight maps in color, a bibliography and an index.

ÉTAT SOCIAL DES PEUPLES SAUVAGES. *Chasseurs. Pêcheurs. Cueilleurs.*
By Paul Descamps. *Payot*
30 francs 5½ x 9; 288 (paper) *Paris*

This book treats the social organization of peoples who are still in the hunting or fishing stage, and especially the influence of their modes of hunting or fishing on other social categories, such as the matriarchate or totemism. M. Descamps finds himself unable to agree with those facile generalizers, the Optimists, that the story of human evolution is a record of universal progress, physical, technical, moral, and intellectual, nor, on the other hand, with the Pessimists that as the arts advance, morals decay. Social evolution, he concludes, is to be figured, not as a linear series, but as a tree with diverging branches. Not all peoples have passed through a totemic phase, nor a boomerang stage, nor a period of cannibalism. The development of each people must be worked out *ad hoc*.

THE DIAGNOSIS OF HEALTH.
By William R. P. Emerson.
D. Appleton and Co.
$3.00 5¼ x 8; xiv + 272 *New York*

This is an interesting and rather annoying book. It is interesting in that it shows at considerable length that a large amount of ill-health, especially in young people, can be remedied by relatively simple measures. It is irritating because one cannot avoid the feeling that health is being judged by an arbitrary yard-stick (weight for height) which makes inadequate allowance for individual variation. We do not accuse Doctor Emerson of this; doubtless in the cases which he handles, individual peculiarities are fully taken account of. But we strongly suspect that when the system is adopted, the school authorities will insist that any child who is under "normal" weight for height is under-nourished, regardless of what other skeletal measurements may show.

MAORI WITCHERY. *Native Life in New Zealand.*
By C. R. Browne. *J. M. Dent and Sons, Ltd.*
$2.00 5⅛ x 7¼; x + 210 *London and Toronto*

Somewhat in the style of fiction, Mr. Browne, who was a government railway surveyor, gives a most interesting account of the domestic manners and customs of the Maoris of New Zealand, as they existed a third of a century and more ago. The book is mainly autobiographical, the author having himself married a Maori girl. The account of the manner in which the witch doctor brought about her death is one of the principal incidents

of the book. One gathers the impression from the book that the Maoris were a fine pagan race before their contact with whites. Their chief intellectual interest appears to have been in *risqué* jokes and stories.

THE BIOLOGICAL BASIS OF HUMAN NATURE.
By H. S. Jennings.
W. W. Norton and Co., Inc.
$4.00 5¾ x 8½; xviii + 384 *New York*

This book is written primarily for the general reader, and has had a great popular success. We liked particularly the chapter on Biological Fallacies and Human Affairs, in which Professor Jennings displays and dissects some of the fallacies which abound in eugenic and other uplift, and which are not altogether unheard of in strictly scientific literature. His discussion of eugenics is fair and sane; we fear that it will hardly be extensively quoted for propaganda purposes by either side. The final chapter, on emergent evolution, left us rather cold. We should have felt better, perhaps, if he had not used as an argument against mechanism that its moral effects are bad. This sounds too much like what we have heard so often from the pulpit.

CHILDREN IN FRUIT AND VEGETABLE CANNERIES. *A Survey in Seven States. United States Department of Labor, Children's Bureau, Publication No. 198. By Ellen N. Matthews.*
U. S. Government Printing Office
40 cents *Washington*
5¾ x 9⅛; vii + 227 (paper)

A survey of child labor in canneries in Delaware, Indiana, Maryland, Michigan, New York, Washington, and Wisconsin. Canning is a highly seasonal industry, employing a high percentage (over one-half) of women, and a considerable number of children. Especially in the eastern states a good deal of migratory labor is employed. Maryland and Delaware show the highest proportion of children under fourteen; they also show the highest percentage of children working a maximum of ten hours or more daily. It appears from the survey that compliance with the child labor laws depends on the energy of the officials charged with enforcement.

CHILD LABOR. *Facts and Figures. United States Department of Labor. Children's Bureau. Bureau Publication No. 197.*
U. S. Government Printing Office
25 cents *Washington*
5¾ x 9⅛; viii + 133 (paper)

This is the third in a series of publications concerned with the analysis of information on the various aspects of child labor. The material, some of which has been previously published, is arranged under five headings, as follows: A history of the movement for the prohibition and regulation of child labor; extent and distribution of child labor in the United States; the causes, social cost, and prevention of child labor; the present legal status of child labor in the United States; vocational guidance and vocational education. A list of reading references is given.

THE ART AND RELIGION OF FOSSIL MAN. *Translated by J. Townsend Russell, Jr.*
By G.-H. Luquet. *Yale University Press*
$5.00 6¼ x 10; xiv + 213 *New Haven*

A short but good and well-illustrated account of Paleolithic art and religion. The chapters on art are much better than those on religion, as is natural; our views on the religion of Paleolithic man are, and

seem likely to remain, very largely based on inference, hypothesis, analogy, and prejudice.

The present author is, as anthropologists go, a cautious man; he rejects a vast deal of cheerful guess-work reasoning about his subject; but a good deal is left which seems to us to go a long way beyond what the facts warrant.

TIZOC, GREAT LORD OF THE AZTECS, 1481–1486. *Contribution from the Museum of the American Indian, Heye Foundation, Vol. VII, No. 4.*
By Marshall H. Saville.
Museum of the American Indian, Heye Foundation
$1.60 6¾ x 10; 78 (paper) *New York*

The author incorporates in this study extracts from the writings of ancient chroniclers and of later students of Aztec history together with a detailed study of the sculptures of the Stone of Tizoc, a very fine golden statuette of this seventh great lord of the Aztecs, and the inscriptions on a tablet of obsidian relating to this period. The work contains many illustrations, numerous notes relating to the text and a list of works consulted. There is no index.

NIEDERSÄCHSISCHE BAUERN. *I. Geestbauern im Elb-Weser-Mündungsgebiet (Börde Lamstedt).*
By Wilhelm Klenck and Walter Scheidt.
Gustav Fischer
8 marks (paper) *Jena*
9.50 marks (cloth)
6¾ x 10⅛; ix + 112 + 8 tables

This intensive study of the peasants of a small district between the estuaries of the Elbe and the Weser is, it is hoped, the first of a series of monographs on the *Rassenkunde* of the German people. After a preliminary sketch of the geography and history of the region, the economic and cultural organization and the physical anthropology of the inhabitants are treated.

VARIATIONS IN DEVELOPMENT AND MOTOR CONTROL IN GOITEROUS AND NON-GOITEROUS ADOLESCENT GIRLS.
By Louise A. Nelson.
Warwick and York, Inc.
$2.75 + 10¢ postage *Baltimore*
5⅛ x 7⅝; xii + 193

Dr. Nelson finds no significant difference between goiterous and non-goiterous girls in ability to inhibit movement or to coordinate eye and hand movements. She concludes that degree of enlargement of the thyroid gland is not a satisfactory measure of its functional activity.

THE U. S. LOOKS AT ITS CHURCHES.
By C. Luther Fry.
Institute of Social and Religious Research
$2.50 6 x 9; xiv + 183 *New York*

An examination of the 1926 Census of Religious Bodies. In addition to discussion of the published data, there is an interesting section on the educational qualifications of ministers, based on material collected but not published by the Census Bureau.

JUVENILE DELINQUENCY IN MAINE. *United States Department of Labor. Children's Bureau Publication No. 201.*
U. S. Government Printing Office
15 cents 5¾ x 9; v + 90 *Washington*

The report of a survey made at the request of the Maine Department of Public Welfare. It consists chiefly of case reports, with a final section of recommendations for getting rid of some more of the taxpayer's money.

DRAMAS OF FRENCH CRIME. *Being the Exploits of the Celebrated Detective René Cassellari.* *Hutchinson and Co., Ltd.*
18 shillings net 6 x 9; 288 *London*

Mildly entertaining stories of the work of the Sûreté Générale. On the whole we prefer to stick to fiction; Sherlock Holmes seems to us a more interesting detective than M. René Cassellari.

THE ANATOMY OF MUSIC. *A Complete Popular Outline of Musical Theory.* *By Winthrop Parkhurst.*
Alfred A. Knopf, Inc.
$2.50 5⅛ x 7½; xix + 200 *New York*

This book is intended to give the music lover who has been content with passive listening enough knowledge of the principles of the subject that, hearing, he may understand.

ZOOLOGY

THE OLIGOCHAETA.
By J. Stephenson.
Oxford University Press
$20.00 6¼ x 9¾; xvi + 978 *New York*

This comprehensive survey of the Oligochaeta will long serve as a source book for zoologists, physiologists and experimentalists. About one fourth of the volume is devoted to classification and bibliography. In the remaining pages the author has gathered together, with much care and discrimination, material which has appeared on the biology of the Oligochaetes within the last 34 years. For earlier results the reader is referred to the monographs of Vejdovsky and Beddard. In the present work not only are the anatomy, histology, embryology and reproduction of these animals discussed but there are included chapters on anomalies of structure, regeneration, ecology and manner of life, geographical distribution, as well as minor subjects. There is even a section on the Oligochaetes in commerce, as food and as medicine. In fact, practically all that is known of the Oligochaetes is to be found within these pages. The author deserves much praise for the arrangement and presentation of the material. His simple and entertaining style makes this part of the book interesting reading even to the layman.

No attempt has been made to deal in a comprehensive manner with the systematic section, the survey stopping at the genera. Likewise in the bibliography of over 1000 items, only systematic papers which furnish data for the general chapters are as a rule included. The book contains many illustrations, also subject and systematic indices. It is a model of monographic writing.

WILD ANIMALS IN AND OUT OF THE ZOO.
By William M. Mann.
Smithsonian Institution Series, Inc.
6¼ x 9⅛; 362 *New York*

This beautifully printed and illustrated volume, by the distinguished Director of the National Zoological Park, is a valuable contribution to the literature relating to zoological gardens, and there are few subjects more fascinating. It forms the sixth volume of the Smithsonian Scientific Series. Unfortunately, as it seems to us, it cannot be separately purchased. The series, which is a private commercial publishing enterprise, must be subscribed to as a whole, and at a price ($198 for the twelve volumes bound in vellum, $150 bound in buckram) which is doubtless not high relatively, considering the quality of the product, but is absolutely great enough to keep the set off the shelves of most working scientific men, in all probability.

Dr. Mann's book is full of entertaining zoo lore, collecting experiences, notes on habits, etc. The history of the National Zoological Park is reviewed, and tables are given in the appendices, showing first the numbers, species, and maximum longevity (in captivity) of all the animals that have ever lived in that zoo; and second, the numbers and species of animals born there. A notable book.

STUDIES OF COMMON FISHES OF THE MISSISSIPPI RIVER AT KEOKUK.
Bureau of Fisheries Document No. 1072.
By Robert E. Coker.
U. S. Government Printing Office
50 cents $7\frac{1}{2}$ x 11; 85 (paper) *Washington*

This survey is restricted largely to those species of fishes of which 50 or more individuals were observed. Special attention is given to their economic importance, breeding habits and range, known or supposed migration, seasonal occurrence and their abundance both before and after the construction of a great dam for hydroelectric power between Keokuk, Iowa, and Hamilton, Illinois. During the course of the survey many problems of considerable significance appeared concerning fishes of the Mississippi River and the author discusses a group of these problems in the concluding pages of his paper. The work contains illustrations of many of the fishes under discussion, charts and tables and a lengthy bibliography. There is no index.

THE LIFE AND LETTERS OF SIR HARRY JOHNSTON.
By Alex. Johnston.
Jonathan Cape and Harrison Smith
$3.50 $5\frac{1}{4}$ x 8; 351 *New York*

Sir Harry Johnston's chief contribution to zoology is his discovery of the Okapi, but throughout his travels and explorations in Africa he was constantly recording his observations and discoveries either with brush or with pen. In these pages we have a highly interesting, if somewhat eulogistic, account of the achievements of this versatile man as scientist, artist and explorer and as fighter, Governor and history maker of Africa.

ANIMAL LIFE OF YELLOWSTONE NATIONAL PARK.
By Vernon Bailey. *Charles C. Thomas.*
$4.00 postpaid *Springfield, Ill.*
6 x $8\frac{3}{4}$; xiii + 241

This is an entertaining book for the layman or the amateur, who intends to visit our most popular national park, to include in his kit-bag. It is devoted chiefly to mammals and birds. Written by a trained naturalist of wide experience, it is accurate. With the exception of the scientific name of each animal which is always given with the common name, the book is devoid of technical terms or descriptions. There are numerous illustrations, a map of the park and an index.

THE FAUNA OF BRITISH INDIA, INCLUDING CEYLON AND BURMA.
Cestoda, Vol. I.
By T. Southwell. *Taylor and Francis*
22 shillings 6 pence *London*
6 x 9; xxxi + 391

In this volume the author has sought to bring together all the information at present obtainable regarding the cestodes of India. He states, however, that the field is largely unexplored. The work is well illustrated and has a lengthy list of references. There are systematic and alphabetical indices.

DIPTERA OF PATAGONIA AND SOUTH CHILE. *Based Mainly on Material*

in the British Museum (Natural History). Part I—Crane-Flies.
By C. P. Alexander.
British Museum (Natural History)
15 shillings *London*
5½ x 8½; xvi + 240 + 12 plates

This monograph is based largely on the collection made by Edwards and Shannon in 1926. The author concludes, from the resemblances to the Australasian fauna, that "the evidence seems overwhelmingly in favour of a former Antarctic land connection."

PRAKTIKUM DER ZÜCHTUNG VON WARMBLÜTERGEWEBE IN VITRO.
By Fritz Demuth.
Rudolph Müller und Steinicke
6 marks (paper) *München*
7.20 marks (bound)
5⅝ x 8⅛; 116

A *vade mecum* for tissue culture workers.

A TEXT-BOOK OF ECONOMIC ZOOLOGY.
By Z. P. Metcalf. *Lea and Febiger*
$4.00 net *Philadelphia*
5¾ x 9⅛; 392

LABORATORY STUDIES IN ZOOLOGY
By H. D. Reed and B. P. Young.
McGraw-Hill Book Co., Inc.
$1.00 5¾ x 9⅛; viii + 121 *New York*

FISCHEREIBIOLOGIE DER ALPENSEEN. *Die Binnengewässer. Band X.*
By Oskar Haempel.
E. Schweizerbart'sche Verlagsbuchhandlung
27.50 marks (paper) *Stuttgart*
29 marks (cloth) 6¾ x 10; viii + 259

OBSERVATIONS ON SOME WYOMING BIRDS. *Scientific Publications of the Cleveland Museum of Natural History, Vol. I, No. 2.*
By Arthur B. Fuller and B. P. Bole, Jr.
Cleveland Museum of Natural History
75 cents *Cleveland*
6⅜ x 9¼; 44 + 10 plates (paper)

A NEW GENUS OF AFRICAN STARLINGS. *Scientific Publications of the Cleveland Museum of Natural History Vol. I, No. 3*
By Harry C. Oberholser.
Cleveland Museum of Natural History
50 cents *Cleveland*
6¼ x 9¼; 2 pages + 2 plates (paper)

NOTES ON A COLLECTION OF BIRDS FROM ARIZONA AND NEW MEXICO. *Scientific Publications, Vol. I, No. 4.*
By Harry C. Oberholser.
Cleveland Museum of Natural History
75 cents 6⅜ x 9⅜; 42 (paper) *Cleveland*

REVISION OF THE FISHES OF THE FAMILY LIPARIDAE. *Smithsonian Institution. United States National Museum. Bulletin 150.*
By Victor Burke.
U. S. Government Printing Office
45 cents *Washington*
6 x 9½; xii + 204 (paper)

BIOLOGICAL PRINCIPLES IN GENERAL ZOOLOGY. *A Laboratory Manual.*
By H. J. Van Cleave, H. R. Linville, and H. A. Kelley. *Ginn and Company*
80 cents 7¾ x 10⅜; vi + 185 *Boston*

ANIMAL MICROLOGY. *Practical Exercises in Zoölogical Micro-Technique.*
By Michael F. Guyer, with a chapter on Drawing by Elizabeth A. (Smith) Bean. Third Edition.
University of Chicago Press
$3.00 6 x 8¾; xiv + 303 *Chicago*

BOTANY

PHYSIOLOGY AND BIOCHEMISTRY OF BACTERIA. *Volume II. Effects of Environment upon Microörganisms. Vol. III. Effects of Microörganisms upon Environment. Fermentative and Other Changes Produced.* *By R. E. Buchanan and Ellis I. Fulmer.*

The Williams and Wilkins Co.

Each volume $7.50 *Baltimore*

All three volumes, ordered at one time, $20.00

5⅞ x 8⅞; Vol. II, xvii + 709

Vol. III, xv + 575

Volumes II and III complete the extensive work, as originally planned by the authors, of compiling and systematizing the great mass of data pertaining to the physiology of microörganisms. Volume I, dealing with *Growth Phases*; *Composition and Biophysical Chemistry of Bacteria and their Environment*; *and Energetics*, has previously been mentioned in these columns. Volume II, devoted primarily to a discussion of the effects of physical and chemical environment upon microörganisms, particularly bacteria, yeasts and molds, is divided into three sections, namely: (1) Effects of environment; their recognition and measurement; (2) Effects of physical environment upon microörganisms; (3) Effects of chemical environment upon microörganisms. In Volume III, the chemical transformations produced by microörganisms are discussed under the headings of (1) Special physiological interrelationships of microörganisms and (2) Effect of microörganisms upon their chemical environment. Both volumes are well documented. Each contains illustrations, a literature list of several hundred titles, subject and author indices as well as an index to microörganisms. To those engaged in the study of general biology as well as bacteriologists this completed work will be indispensable. It is a notable contribution to American biological scholarship.

THE PRINCIPLES OF BACTERIOLOGY AND IMMUNITY. *In two volumes.* *By W. W. C. Topley and G. S. Wilson.*

William Wood and Co.

$15.00 net *New York*

per set

6½ x 9½; xliv + 1300

It has been the aim of the authors to supply a text-book for those advanced students of medicine and biology who wish to make a comprehensive study of bacteriology and in particular its application to the problems of infection and resistance. Parts I and II, of Volume I, deal with the general and systematic aspects of the subject, while Parts III and IV, of Volume II, are devoted to "Infections and Resistance," and the "Application of Bacteriology to Medicine and Hygiene." The work bears evidence of much labor and meticulous care in its preparation. It is adequately illustrated. Reference lists, frequently lengthy, are appended to each chapter. There is an excellent index for each volume.

COMPARATIVE STRENGTH PROPERTIES OF WOODS GROWN IN THE UNITED STATES. *United States Department of Agriculture Technical Bulletin No. 158.* *By L. J. Markwardt.*

U. S. Government Printing Office

10 cents *Washington*

5¾ x 9⅛; 39 (paper)

This bulletin is based in part upon an earlier publication issued by the U. S. Department of Agriculture on "Mechanical properties of woods grown in the United States." It gives comparative figures for weight, shrinkage and strength of 164 native species, explanations of the

eleven different tests made, and their applicability. For those who wish additional information concerning the use and derivation of the figures given there are three appendices under the following headings: (a) "Strength of structural material," (b) "Method of computing comparative strength and shrinkage figures," and (c) "Significance of variability." Seven tables are included in the text, together with formulae for calculating various strength properties. There is a brief literature list.

GNETALES.
By H. H. W. Pearson. *The Macmillan Co.*
$6.00 7 x 10¼; vii + 194 *New York*

This monograph on a curious class of plants, posthumously published, and edited by A. C. Seward, concludes that the relationship of the three genera composing it to each other and to other groups is still obscure but "that in spite of the appearance in them of certain Angiosperm characters, they are essentially Gymnosperms."

THE PROTEASES OF PLANTS. *A Record and a Reply.*
By S. H. Vines. *Macmillan and Co.*
1 shilling net *London and New York*
5⅜ x 8½; 32 (paper)

A summary of the author's work on plant enzymes and a defense, as against Willstätter, of his conclusion that two enzymes are involved in the digestion of protein by plant-extracts.

BACTERIOLOGY. *A Text Book on Fundamentals.*
By Stanley Thomas.
McGraw-Hill Book Co., Inc.
$3.00 5¾ x 9; xv + 301 *New York*

A second edition entirely rewritten but maintaining the plan of the first edition. There is an additional chapter on the morphology and physiology of bacteria.

THE OEDOGONIACEAE. *A Monograph Including all the Known Species of the Genera Bulbochaete, Oedocladium and Oedogonium.*
By Lewis H. Tiffany. *Lewis H. Tiffany*
$4.00 (paper) *Columbus, O.*
$5.00 (cloth)
6¾ x 10; 253

It is hoped that this excellent monograph will be followed by similar ones on other groups of filamentous algae.

ACTA FORESTALIA FENNICA 35 and 36.
6⅜ x 9½; 464 and 506

SILVA FENNICA 13. *Om Skogars Skötsel i Norden.*
By C. C. Bocker.
6½ x 10; 129

SILVA FENNICA 14. *A Short Account of the History of the Forestry of the Jokioinen Estate.*
By O. Tähtinen.
6¼ x 9¾; 50

SILVA FENNICA 15. *Wesen und Bedeutung der Waldtypen.*
By A. K. Cajander.
6¼ x 9¾; 66

SILVA FENNICA 16. *The Promotion of Higher Education in Agriculture and Forestry in Suomi.*
6¼ x 9¾; 92

COMMENTATIONES FORESTALES 3. *Neue Waldsaatmethode (Vorläufige Mitteilung).*
By K. Melders.
6¼ x 9¾; 16

COMMENTATIONES FORESTALES. *Le Prof. Dr. A. K. Cajander et ses Mérites Scientifiques dans le Domaine de la Typologie*

Forestière. (A l'Occasion du Cinquantiéme Anniversaire de sa Naissance.)
By Jean Miklaszewski.
$6\frac{1}{4}$ x $9\frac{3}{4}$; 22
Society of Forestry in Suomi
Helsingfors, Finland

A TEXTBOOK OF BOTANY. *Revised for Colleges and Universities. Vol. I, Morphology. Vol. II, Physiology.*
By John M. Coulter, Charles R. Barnes and Henry C. Cowles.
American Book Co.
$1.80 net for each volume *New York*
$5\frac{1}{2}$ x $8\frac{1}{4}$; Vol. I, viii + 310
Vol. II, viii + 307

COLLEGE BOTANY. *With Special Reference to Liberal Education.*
By George B. Rigg. *Lea and Febiger*
$4.00 net $5\frac{1}{4}$ x $7\frac{3}{4}$; 442 *Philadelphia*

BACTERIOLOGY. *For Students in General and Household Science. Third Edition.*
By Estelle D. Buchanan and Robert E. Buchanan. *The Macmillan Co.*
$3.00 5 x $7\frac{3}{4}$; xvi + 532 *New York*

MORPHOLOGY

AN INTRODUCTION TO VERTEBRATE EMBRYOLOGY.
By H. L. Wieman.
McGraw-Hill Book Co., Inc.
$4.00 $5\frac{3}{4}$ x 9; xi + 411 *New York*

This book is especially designed for premedical students but will be found useful in general courses in embryology. While mainly concerned with chick and pig embryos, much attention is given to general cytology, cleavage and early stages in *Amphioxus* and the frog, and organogenesis in the human embryo. The comparative point of view is maintained throughout the text. The many illustrations are well executed and there is a bibliography and an index.

LES PLEXUS CHOROÏDES. *Anatomie, Physiologie, Pathologie.*
By Nathalie Zand. *Masson et Cie*
22 francs *Paris*
$6\frac{1}{2}$ x 10; viii +140 (paper)

In this careful monograph the author concludes that the choroid plexuses secrete the cerebrospinal fluid and serve with the meninges as a protective barrier against harmful substances dissolved in the blood. She does not find grounds for supporting the opinion of von Monakow that lesions of the choroid plexuses are the cause of schizophrenia.

VERTEBRATE EMBRYOLOGY. *A Textbook for Colleges and Universities.*
By Waldo Shumway.
John Wiley and Sons, Inc.
$3.75 net $5\frac{7}{8}$ x 9; x + 311 *New York*

A second, revised edition of a widely used text book.

LABORATORY GUIDE TO VERTEBRATE DISSECTION. *For Students of Anatomy.*
By A. B. Appleton. *The Macmillan Co.*
$2.40 $4\frac{3}{4}$ x $7\frac{1}{4}$; xix + 152 *New York*

The price of this book as given in Volume V, Number 4, page 480, of THE QUARTERLY REVIEW OF BIOLOGY, is incorrect.

PHYSIOLOGY AND PATHOLOGY

SOME ASPECTS OF THE CANCER PROBLEM. *An Account of Researches into*

the Nature and Control of Malignant Disease Commenced in the University of Liverpool in 1905, and Continued by the Liverpool Medical Research Organization (Formerly the Liverpool Cancer Committee), Together with Some of the Scientific Papers that Have Been Published. Edited by W. Blair Bell.

William Wood and Co.

$20.00 $7\frac{1}{4}$ x $10\frac{3}{8}$; xiv + 543 *New York*

This book consists largely of a collection of previously published papers by Bell and his co-workers, embedded in an editorial stroma. The working hypothesis on which their researches have been based is that malignant growths are a reversion of normal tissue to a type resembling the chorionic epithelium. This is indicated by histological, chemical and physiological likenesses. Since lead has "an almost specific action on the chorionic epithelium," its effect on malignant tumors was tried. Of 566 cases treated, 304 "received more than one-half of the minimum treatment advised," and in 65 cases, or 21 per cent of the 304, the disease was completely arrested or believed cured. Bearing in mind "the serious type of case for the most part treated," Bell considers this an encouraging result. There is a bibliography of 665 titles and an index.

REFLEX ACTION. *A Study in the History of Physiological Psychology. By Franklin Fearing.*

The Williams and Wilkins Co.

$6.50 6 x 9; xiv + 350 *Baltimore*

A book of much interest and importance. The author divides the history of the development of the reflex arc concept into five periods, as follows: the pre-scientific period, the speculative period, the period of nascent experimentation, the period of the development of knowledge regarding the structural components of the reflex arc, and the modern period. The first eleven chapters deal with the first four periods while the last five chapters deal with the fifth period. Only those phases of the subject are discussed which are related directly to reflex action as an explanatory principle in physiological psychology. The work includes a bibliography of 554 titles, and name and subject indices.

AN ELEMENTARY COURSE IN GENERAL PHYSIOLOGY. *Part I—Principles and Theory*, by G. W. Scarth. *Part II—Laboratory Exercises*, by F. E. Lloyd and G. W. Scarth.

John Wiley and Sons, Inc.

$2.75 $5\frac{3}{4}$ x 9; xxi + 258 *New York*

This excellent introduction to the physiology of plant and animal life is the outgrowth of a series of laboratory exercises used by the author in a course in general physiology. The book will be found highly useful in general biology and premedical courses. It is divided into two parts. The principles and theory of the general properties and behavior of cells are discussed in the first part. Suggested readings for more exhaustive studies of the topics discussed are given for each chapter. The second part of the book is devoted to exercises for laboratory work. It is so arranged that some of the more advanced work can be easily eliminated. The book is illustrated and indexed and includes a section on apparatus and materials.

IMMUNITY IN INFECTIOUS DISEASES.

By A. Besredka. Authorised Translation by Herbert Child.

The Williams and Wilkins Co.

$5.00 $5\frac{1}{2}$ x $8\frac{1}{2}$; vii + 364 *Baltimore*

The author of this book, widely known

for his researches on vaccines, prefers to present his work in the form of "A Series of Studies," since the rapid progress of the science of immunity is so constantly producing new discoveries and theories. The fifteen chapters deal with experimental problems and results covering a period of thirty years work at the Pasteur Institute bearing on different aspects of the general problem of immunity. Much space is devoted to discussing critically the value of the researches of various investigators and the bearing which these have had upon the development of the science of immunity. A valuable and stimulating book to place in the hands of students who wish to do general reading in this field. It is well documented.

BREAD. *A Collection of Popular Papers on Wheat, Flour and Bread.*
By Harry Snyder. With Biographical Sketch by Andrew L. Winton.
The Macmillan Co.
$2.50 5⅛ x 7¾; x + 293 *New York*

A collection of papers boosting white flour and bread. The author was at one time professor of agricultural chemistry in the University of Minnesota, and was later associated with a flour-milling concern in Minneapolis. Reginald, the office boy, says that he likes white bread better, too, and has been memorizing passages for use in arguing with his mother, who is a great believer in vitamins and things.

MAMMALIAN PHYSIOLOGY. *A Course of Practical Exercises. A New Edition. By E. G. T. Liddell and Sir Charles Sherrington.*
Oxford University Press
$4.00 8 x 10⅞; xii + 162 *New York*

A series of experiments on decapitate or decerebrate mammalian preparations, which should offer a welcome change from the plague of frogs. The book is excellently done; the illustrations are much better than we are accustomed to in a laboratory manual; the instructions are clear and helpful; and the annotations should give the student an historical orientation of value.

MEDICAL AND SURGICAL YEAR-BOOK. *Physicians Hospital of Plattsburgh. Comprising Wednesday Afternoon Invitation Lectures, Papers of the Cardiac Round Table, The First Beaumont Lecture, Collected Papers by the Staff.*
The Superintendent, Physicians Hospital of Plattsburgh
$3.50 *Plattsburgh, N. Y.*
6 x 9¼; xv + 322

A collection of lectures and papers, largely on cardiovascular-renal diseases, but also including an address at the unveiling of a memorial tablet to Dr. William Beaumont, and papers on pneumonia, congenital syphilis, gall-bladder disease, adrenal insufficiency, pulsating exophthalmos, pathologic labor, gas bacillus infection, pulmonary cancer, anesthetics, x-ray examination of teeth, gastric ulcer and carcinoma, bronchoscopy, and agranulocytic angina.

REVIEW OF CARBON MONOXIDE POISONING. *Public Health Bulletin No. 195.*
By R. R. Sayers and Sara J. Davenport.
U. S. Government Printing Office
20 cents *Washington*
5¾ x 9⅛; iii + 97 (paper)

This survey deals with the occurrence and symptoms of carbon-monoxide poisoning; its diagnosis; the percentages of carbon-monoxide dangerous to breathe, and the pathology, prevention and treat-

ment of carbon-monoxide poisoning. There is a bibliography of 195 titles.

SENSATION AND THE SENSORY PATHWAY.
By John S. B. Stopford.
Longmans, Green and Co.
$3.00 5½ x 8½; xii + 148 *New York*

An account of our present knowledge of the sensory paths and centers of the peripheral and central nervous system.

LA RATE. *Organe Réservoir.*
By Léon Binet. *Masson et Cie*
20 francs 6⅛ x 9¼; 117 (paper) *Paris*

An experimental study of the functions of the spleen, especially as a blood reservoir.

LABORATORY MANUAL IN COLLEGE PHYSIOLOGY.
By Cleveland P. Hickman. *The Macmillan Co.*
$1.10 5 x 7½; xiv + 116 *New York*

BIOCHEMISTRY

THE MATERIALS OF LIFE. *A General Presentation of Biochemistry.*
By T. R. Parsons.
W. W. Norton and Co., Inc.
$3.00 5¾ x 8¼; 288 *New York*

As this interesting exposition of biochemistry is aimed at the general reader, it is written without using chemical formulas. The greater part of the book deals with nutrition, but there are also chapters on the chemistry of muscular exercise, blood chemistry, vitamins, endocrine secretions, and the cycle of nature. There is a list of suggested reading and an index.

NEWTON, STAHL, BOERHAAVE ET LA DOCTRINE CHIMIQUE.
By Hélène Metzger. *Félix Alcan*
40 francs 5½ x 9; 332 (paper) *Paris*

An account and examination of the chemical theories of Newton, Stahl, and Boerhaave, written largely with a view to establishing their relations to Lavoisier. The book is a valuable contibution to the history of chemistry. The index is noteworthy in that it supplies a line or two of biographical information about the authors cited.

DIE GLOBULINE.
By Mona Spiegel-Adolf. *Theodor Steinkopff*
33 marks (paper) *Dresden*
35 marks (cloth)
6¼ x 9½; xv + 452

This exhaustive monograph, the fourth volume of the *Handbook of Colloid Science* edited by W. Ostwald, treats the chemistry, physical chemistry, and biological and medical aspects of this important class of proteins.

INTRODUCTION TO PHYSIOLOGICAL CHEMISTRY.
By Meyer Bodansky.
John Wiley and Sons, Inc.
$4.00 5¾ x 9; ix + 542 *New York*

A second edition, rewritten and enlarged. Two new chapters have been added, one dealing with the composition of food stuffs and the other with the composition of milk and certain tissues.

DIE CHEMIE DER CEREBROSIDE UND PHOSPHATIDE.
By H. Thierfelder and E. Klenk.
Julius Springer
19.60 marks (paper) *Berlin*
21.20 marks (bound)
5½ x 8½; viii + 224

This monograph on two important classes of lipoids will be useful to the biochemist.

SEX

GENERATIONS OF ADAM.
By A. L. Wolbarst. *Newland Press*
$3.50 5½ x 8; ix + 355 *New York*

This is a book which no Christian mother should put in the hands of her child. Its point of view is indicated by its preface: "It aims to emphasize the sharp line of demarcation between the biology of sex as ordained by Nature, or God, as you prefer, and the religious or moral concept of sex so vigorously and tenaciously fostered by theology; it seeks to eliminate from our social consciousness the doctrine that sex and sin are synonymous and inseparable,—in other words, to divorce sin from sex."

The author has attempted to treat his subject realistically and rationally. The result is vastly superior to most of what gets into print about sex in books designed for the general public.

THE INTERNAL SECRETIONS OF THE OVARY.
By A. S. Parkes. *Longmans, Green and Co.*
$7.50 5¾ x 8⅝; xv + 242 *New York*

In this book the author brings together the more important facts bearing upon the internal secretions of the ovary. Considerable space is devoted to the morphological aspects of the oestrous cycles in those species where it has been studied in some detail. In the sections dealing with the endocrine control of the female reproductive organs the author gives a very complete discussion of the various phases of the problem, including much experimental data. A valuable part of the monograph is the bibliography of 661 titles. The work includes many excellent illustrations and tables and diagrams of growth curves and oestrous cycles. There are author and subject indices. Students and investigators interested in the physiology of the endocrine organs will find this a notable addition to the literature of their field.

BIOMETRY

INTRODUCTION TO MEDICAL BIOMETRY AND STATISTICS.
By Raymond Pearl. *W. B. Saunders Co.*
$5.50 net 6 x 9⅛; 459 *Philadelphia*

This second edition of this well-known textbook is revised and enlarged, and to a considerable extent rewritten in the light of seven years' experience of its use in the class-room. Among the additions are a section on the nature of statistical knowledge; a more detailed discussion of the census method; the fourth decennial revision (1929) of the International List of Causes of Death, including the Intermediate and Abridged Lists and recommendations of the International Commission; sections on the making of scientific records; record forms; a life table nomogram; applications of the corrected rate principle; a more detailed treatment of the chi-square test; the graphic representation of relative variability; and a chapter on the logistic curve.

THE GREAT MATHEMATICIANS.
By H. W. Turnbull. *Methuen and Co., Ltd.*
2s. 6d. 4⅛ x 6⅞; viii + 128 *London*

A brief account of some of the great mathematicians. The author has attempted to tell the story without the use of mathematical symbolism, and has, on the whole, succeeded surprisingly well.

Naturally, perhaps, the best chapters are the earlier ones, and especially those dealing with the Greeks; it is much less difficult to give a popular account of elementary geometry than of the geometry of Riemann. In general, the names which appear are well chosen, though omissions will probably occur to many readers. For example, the relation of Barrow to Newton and the differential calculus is completely passed over.

PSYCHOLOGY AND BEHAVIOR

HUMAN SPEECH. *Some Observations, Experiments, and Conclusions as to the Nature, Origin, Purpose and Possible Improvement of Human Speech.*
By Sir Richard Paget.

Harcourt, Brace and Co.
$6.00 5½ x 8⅓; xiv + 360 *New York*

The more interesting and important portions of this book are those dealing with the author's experimental researches into the nature of speech sounds. He has succeeded in producing artificially nearly all the sounds of English speech, both consonant and vowel. He finds that both consonants and vowels are essentially double resonance phenomena, the consonants being also characterized by the change and rate of change of pitch produced by alterations in one of the orifices of the resonators.

When he comes to deal with the origin of speech, he is on less firm ground. He holds to the "gesture theory" of the origin of speech—that is, that speech originated in lingual and buccal gestures simultaneous with and imitative of manual gestures. Whether this is the true origin of speech we do not profess to know; but we feel that the evidence here offered is wholly inadequate to establish its plausibility.

DIRECTION ORIENTATION IN MAZE RUNNING BY THE WHITE RAT. *Comparative Psychology Monographs, No. 32.*
By J. F. Dashiell.

The Johns Hopkins Press
$1.50 6¾ x 10; 72 (paper) *Baltimore*

An important contribution to studies in animal learning. The rats in these experiments exhibited a "general orientation function" which successfully served them in solving their problems of maze running. The author found that

> Instead of learning one pathway-pattern to the goal by the often-stated process of (a) chancing upon a certain way that turned out to be adaptive or successful and then (b) fixating this way by tending to repeat it more and more—our animals *learned to become adjusted in some more general manner, directionally*, which more general adjustment then served as *a steering or influencing factor operative somewhat independently of the purely local stimuli encountered* by the rat and so serving to guide it *even when tracing pathways never before entered.*

Various contemporary studies and theories are examined and discussed by the author in seeking an interpretation of these results but, none seeming adequate, the following suggestion is offered as a possible explanation.

> When a rat first enters the maze there may be set up some kind of kinesthetic or organic posturing or set (developed in preceding trials), determined by the animal's position when proceeding up the entrance passage way. Then, as the animal traverses the maze and encounters obstacles forcing it to turn right or left, a persisting segment of the initial orientation may inhibit specific stepping movements antagonistic to it and facilitate those consonant with it.

The report includes illustrations of rat performance in maze routes, tables of runs, etc. and a bibliography.

PREFERENTIAL MANIPULATION IN CHILDREN. *Comparative Psychology Monographs, No. 33.*

By Julia H. Heinlein.

The Johns Hopkins Press

$1.75 7 x 10; 121 (paper) *Baltimore*

In this investigation on 36 children of pre-school age at the Child's Institute of the Johns Hopkins University, the author states that the results

> of the various tests of handedness seem to indicate the existence of "degrees" of manual bias ranging from a pronounced preference for either the right hand or the left hand, to a relatively ambidextrous state in which neither hand is definitely favored, or in which the hand "convenient" under the circumstance is favored. The two manual types designated conventionally as "right-handed" and "left-handed" apparently indicate "trends" rather than two distinct classes, at least in so far as activities of the type used in these tests are concerned.

It is interesting to note that there was marked indication that the training gained in a series of practice tests for the non-preferred hand in a group of "right-handed" children was transferred when the tests were presented to the same children for "right-handed" performance. On the other hand

> performances of the majority of the children in the left-handed group did not show a marked tendency toward improvement in either the practiced right hand or the unpracticed left hand, although there was some individual variation.

In addition to the manual tests, the preferential use of hands by the children of the pre-school group was daily under observation and yielded significant results. The author includes in her report tables showing the results of the tests and a bibliography of 16 titles.

SYSTEMATIC PSYCHOLOGY: PROLEGOMENA.

By Edward B. Titchener.

The Macmillan Co.

$2.50 $4\frac{7}{8}$ x $7\frac{3}{8}$; xi + 278 *New York*

Although only a fragment of what the author intended to be his *magnum opus*, this book is an important contribution to the foundations of psychology. In formulating his definition of psychology Professor Titchener found it necessary to consider the essential character of science in general and of physics and biology in particular. The definitions of the three sciences at which he arrives are as follows:

> *Psychology* is the science of existential experience regarded as functionally or logically dependent upon the nervous system (or its biological equivalent);
> *Biology* is the science of existential experience regarded as functionally or logically dependent upon the physical environment; and
> *Physics* (including chemistry and physical chemistry) is the science of existential experience regarded as functionally or logically interdependent.

THE MEANING OF SACRIFICE. *Thesis Approved for the Degree of Doctor of Philosophy in the University of London. The International Psycho-Analytical Library No. 16.*

By R. Money-Kyrle. The Hogarth Press

18 shillings $6\frac{1}{4}$ x $9\frac{1}{2}$; 273 *London*

The author finds Freud's theory of the origin of sacrificial rites from the Oedipus complex a more adequate explanation of the different forms of sacrifice actually observed than other theories. He points out, however, that the assumption of the inheritance of acquired memory made by some of Freud's followers is both dangerous and unnecessary. "Sacrifice may be regarded, less as the result of a primeval crime, than as the symbolic expression of an unconscious desire for parricide which each individual has himself acquired."

THE GROWING BOY. *Case Studies of Developmental Age.*

By Paul H. Furfey. The Macmillan Co.

$2.00 5 x $7\frac{1}{2}$; ix + 192 *New York*

Doctor Furfey gives here the results of his studies of the personality and interests

of boys from six to sixteen years old. He finds a normal development from the dramatic play of the six-year-old through the gang age (from ten to fourteen) to adolescence. There are, however, individual variations in the rate of this development which lead him to the concept of developmental age. Thus a boy of ten who retains the play activities characteristic of the eight-year-old has a developmental age of eight and a developmental quotient of 80. Developmental age is not correlated with mental age, but there is a small correlation with weight and height.

READINGS IN PSYCHOLOGY. *By Raymond H. Wheeler. With special readings by Harry Helson, Milton Metfessel and Thomas D. Cutsforth.* *Thomas Y. Crowell Co.*
$3.75 5½ x 8½; x + 597 *New York*

A collection of papers, designed for collateral reading for a first course in psychology. The papers, largely experimental in character, are selected to illustrate and support the "organismic" view of the editor, which seems to be fundamentally that of the Gestalt school.

NINTH INTERNATIONAL CONGRESS OF PSYCHOLOGY, *Held at Yale University, New Haven, Connecticut, September 1st to 7th, 1929, under the Presidency of James McKeen Cattell. Proceedings and Papers.* *The Psychological Review Co.*
$5.25 7 x 10¼; xli + 534 *Princeton, N. J.*

Contains abstracts of papers read, together with addresses by various officials of high degree.

DE OMNIBUS REBUS ET QUIBUSDEM ALIIS

NEW FRENCH COOKING. *300 New and Unique Recipes. By Paul Reboux. Translated from the French by Elizabeth Lucas.* *Alfred A. Knopf, Inc.*
$2.50 5 x 7½; xiii + 263 *New York*

FRENCH COOKING FOR ALL. *By Gaston Voisin.* *Frederick A. Stokes Co.*
$2.00 5 x 7⅜; 187 *New York*

There appears to be a considerable present interest on the part of the great American public in French food and cooking, if one may judge from the activity of publishers in catering to it. What is the cause of so noble an elevation in the public taste above the hitherto current hog and hominy, pork and beans, and baking powder biscuit level of gastronomy has not been revealed, but in any case it is worthy of all praise and pious giving of thanks to God and Brillat-Savarin.

The two books before us lie at the opposite poles of merit. M. Reboux's treatise is probably the most original and entertaining work on gastronomy to appear in English, while M. Voisin's (there is no evidence of any connection with the illustrious *restaurateur* of that name) is nearly worthless. The measure of its authoritativeness is given by the fact that it solemnly describes the preparation of *champignons à la Provençale* without any mention of garlic at any stage! No more need be said of such a misguiding, debased, pernicious, and futile book.

Paul Reboux is one of the most original and versatile of living Frenchmen. He has been a poet, a newspaper editor (*Paris-Soir*), a political writer, a columnist,—all with brilliant success. His post-war book *Les Drapeaux* was, in our opinion, the soundest and most penetrating book ever written on patriotism. If the advice he gave in it had been heeded the story of Europe during the decade just passed would have been a very different one. Now he appears as a *gastronome*. This book is delightful. His recipes are adorned with brilliantly witty comment, and they are of an originality. Food and

drink are, of course, preeminently matters of taste, upon which universal agreement is neither to be expected nor desired. We, for example, while observing much in Reboux's gastronomic philosophy that is admirable, cannot follow him in his passion for bananas, a food obviously intended by the Almighty for *Drosophila* but not for man. But on the other hand his ideas about the making of a duck *pâté* are plainly inspired.

No biologist (or other civilized person) should be without this book.

TYPES OF PHILOSOPHY.
By William Ernest Hocking.
Charles Scribner's Sons
$2.50 5½ x 8⅛; xv + 462 *New York*

"Every instructor, whatever his subject, conveys a philosophy; the teaching of English, of history, of economics, of science is at the same time a teaching of philosophy, if only because the instructor is a man and cannot help communicating himself *via* his subject." Hocking has prepared a valuable summary and discussion of the types of philosophy for the thinking man and for the beginner in the study of philosophy. In this book the author combines the historical with the systematic treatment of the subject. There is a careful selection of the types of philosophy from the standpoint of "the validity of the world view, not in the historic rôle." This makes the book valuable not only for the beginner but also for the seasoned student of philosophy and for the scientist, because it presents an argument in the sequence of types, which, in its simplicity of presentation, preserves "first Principles." The chief types of philosophy discussed are spiritualism, naturalism, pragmatism, intuitionalism, dualism, idealism, realism, and mysticism, in the order named. They are offered as philosophies contributing towards a synthetic world view rather than as competing systems of philosophic thought. This approach is especially useful for the scientist and teacher, who wishes to orient his thinking in relation to his field of science, and to assist in clarifying his concepts toward a synthetic philosophy of his own. Hocking closes with his own *confessio fidei*. This book is well worth the consideration of the biologist. There are lists of numerous, selected references, classified for student use, accompanying the discussion of each type. Subject and name indexes are printed separately.

A PRACTICAL MEDICAL DICTIONARY *of Words Used in Medicine with Their Derivation and Pronunciation, Including Dental, Veterinary, Chemical, Botanical, Electrical, Life Insurance and Other Special Terms; Anatomical Tables of the Titles in General Use, and Those Sanctioned by the Basle Anatomical Convention; Pharmaceutical Preparations, Official in the U. S. and British Pharmacopoeias and Contained in the National Formulary, and Comprehensive Lists of Synonyms.*
By Thomas L. Stedman.
William Wood and Co.
$7.50 net 6 x 9½; xi + 1220 *New York*

SHORT TALKS ON SCIENCE.
By Edwin E. Slosson. *The Century Co.*
$2.00 5 x 7¼; xii + 281 *New York*

A collection of brief notes, largely reprinted from the weekly journals, touching on topics from bacteriology to physics. It reminds us strangely of Mr. Ripley's "Believe it or not," but others may differ.

THE REVOLT AGAINST DUALISM. *An Inquiry Concerning the Existence of Ideas. By Arthur O. Lovejoy.*

W. W. Norton and Co., Inc.

$4.00 6 x 9; xii + 325 *New York*

In this analysis of the realistic-monistic movements of the past quarter century, Dr. Lovejoy concludes that they are either inadequate or essentially dualistic under the disguise of a novel terminology. If this distinguished author would only write as simply, lucidly, and forcefully as he speaks, this important book would be assured of a wider audience than it will probably get.